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ABSTRACTS

"EFFECTIVENESS AND SAFETY OF THERAPEUTICS: DEALING WITH TRANSPARENCY, MINIMIZING BIAS, AND IMPROVING KNOWLEDGE TRANSLATION TO CONCERNED STAKEHOLDERS"

May 6th – 8th, 2012
Montreal, Quebec
The Hyatt Regency Hotel

CAPT ACTP

The Canadian Association for Population Therapeutics /
Association Canadienne pour la Thérapeutique des Populations

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CAPT SUBMITTED ABSTRACTS

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ORAL PRESENTATIONS

(Note: Presenting Authors are underlined)

1

A review of instruments measuring patient attitudes toward antidiabetic drug therapy

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Background: Several psychosocial interventions are developed to improve adherence to medication for chronic conditions. Understanding the process through which these interventions could improve adherence is essential. Patient attitudes toward medication defined as the frame of mind with respect to medication, represent one of these potential process variables that could be measured in trials testing adherence interventions.
Objective: To identify and evaluate instruments measuring patient attitudes toward antidiabetic drugs (AD) among adults with type 2 diabetes (T2DM).
Methods: We carried out a systematic review. We searched PubMed until 05/2011 for instruments including items on attitudes toward AD in adults with T2DM. We included instruments available in French or English and excluded instruments with less than 50% of items on attitude toward AD. For each instrument, we extracted the following data: purpose, source and selection of items and psychometric properties (reliability, validity, responsiveness). This data was used to evaluate the quality of instruments.
Results: We included 24 instruments of which 10 focused exclusively on attitudes toward AD. Aspects of patient attitudes considered were mainly beliefs, self-efficacy and satisfaction. Seventeen had a good development process (purpose described, two-or-more sources for item development, two-or-more types of approaches for item selection), but only six were considered good regarding validation (Cronbach alpha >0.60, item total correlation >0.2 or ICC >0.50, correlations with other constructs concordant with a priori hypotheses). None has been validated for responsiveness.
Conclusion: This review can assist researchers in selecting instruments with higher levels of reliability and validity and appropriate for their study.
Keywords: *Questionnaire, medication, type 2 diabetes*

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Adherence to antidiabetic drug treatment among workers with type 2 diabetes

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Background: Adherence to the antidiabetic drug (AD) treatment may lessen deleterious effects of Type 2 diabetes on productivity at work.
Objectives: In workers initiating an oral AD treatment, 1) to assess the proportion of individuals persistent with their treatment one year after its initiation, 2) among those persisting, to assess the proportion of compliant individuals, 3) to identify the determinants of persistence and 4) of compliance.
Methods: We performed a cohort study using the RAMQ databases. We included adults insured by the public drug plan who had initiated an oral AD between 2000/01/01 and 2008/12/31. Retired individuals and those on welfare were excluded. Individuals who had a claim for any AD in the 45 days preceding the anniversary or their first claim were deemed persistent. Among them, were considered compliant those who had a supply of AD for at least 80% of the days. Multivariate logistic regression models were used to identify characteristics associated with both outcomes.
Results: Among the 41,006 study individuals, 81.1% were persistent, and 69.7% of those who persisted were compliant. Older individuals, those living in a rural area,

with a higher number of pharmacy visits or who had past compliance with cardioprotective treatments were more likely to be both persistent and compliant, whereas those initially on a sulfonylurea or who had consulted a physician ≥14 times in the year before initiating treatment were less likely to be persistent and compliant.
Conclusions: Identified determinants could help tailoring interventions aimed at optimizing the use of OAD treatments.
Keywords: *Adherence, diabetes type 2, workers*

3

Are deep venous thrombosis events accurately identified using administrative databases? A systematic review

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Funding Source: Canadian Arthritis Network

Background: Deep venous thrombosis (DVT) represents a major health burden. Some authors have attempted to assess the risk of DVT at the population level using health services administrative databases. However, since administrative databases were not intended for research purposes, one may question the quality of such data. Our objective was to review the literature to determine the accuracy of the diagnoses of DVT in administrative databases.
Methods: We searched Medline and Embase to retrieve validation studies of DVT diagnoses based on administrative data. We recorded the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of DVT diagnoses reported by each study.
Results: A total of 13 articles were retrieved. The number of identified DVT events in studies ranged from 32 to 8,923. There was a wide variation in the estimates of sensitivity for various DVT algorithms, ranging from 11% to 87% (median: 61%). The PPV estimates of DVT coding varied from 71% to 88% in 7 studies (median: 84%); the 2 studies that presented estimated lower values (18-31%) focused solely on DVT as side effect of surgery. Specificity and NPV were evaluated in 2 studies and were high (97% to 100%).
Conclusions: Sensitivity was low-to-moderate in most studies, which could result in misleading rates of DVT incidence in studies using administrative databases. PPV was generally moderate to high, indicating a good ability to confirm DVT. However, to specifically identify DVT as a complication of surgery, information other than administrative data may be necessary
Keywords: *Deep venous thrombosis, systematic review, administrative databases*

4

Beware of policy-induced selection bias in drug effect studies: example in the comparative effectiveness of oral bisphosphonates

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Funding Source: Canadian Institutes of Health Research

Background: Oral bisphosphonates are effective in reducing vertebral fracture risk, however, only alendronate and risedronate have proven efficacy in reducing hip fracture risk.
Methods: We examined the comparative effectiveness of oral bisphosphonates in reducing hip fracture risk among new users in British Columbia (BC) and Ontario, 2001/02-2008/09. BC data included all drugs dispensed in community pharmacies. Ontario data included drugs covered through the public plan that largely restricted alendronate and risedronate to those with lower bone mineral density. Sex- and province-specific Cox-proportional hazards models, matched on propensity score derived from claims data were used to compare 1-year hip fracture rates between exposures. Alendronate was the referent in all comparisons.
Results: We identified little difference in fracture rates between etidronate or risedronate and alendronate among men and women in BC, or among women in Ontario. We similarly identified little difference in fracture rates between risedronate and alendronate (HR=0.94; 95%CI=0.79-1.16) among men in Ontario. However, we identified lower hip fracture rates among men in Ontario treated with etidronate vs. alendronate (HR=0.75; 95%CI=0.59-0.95).
Conclusions: We identified little difference in the effectiveness of alendronate or risedronate in reducing hip fracture risk among men or women. Despite being matched on measured risk factors for fracture, results suggest that residual confounding persisted with fracture rates lower among men in Ontario treated with etidronate vs. alendronate - a finding contrary to placebo-controlled evidence. Careful attention to province-specific drug restriction policies is important as Canada builds its drug safety and effectiveness network.
Keywords: *Bisphosphonate, drug policy, fracture, osteoporosis, pharmacoepidemiologic methods*

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Cost-effectiveness of intravenous thrombolysis compared to best medical treatment for late-presentation acute ischemic stroke in an Ontario setting

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Background: For late-presentation ischemic stroke patients, economic evidence comparing currently employed treatment strategies is lacking. We evaluated the cost-effectiveness of intravenous thrombolysis compared to best medical treatment in late-presentation patients suffering an acute ischemic stroke in an Ontario setting.
Methods: A probabilistic economic model was designed from the perspective of a government payer to calculate the lifetime incremental costs and quality adjusted life years (QALYs). Functional independence and mortality were extracted from randomized trials. Discharge disposition was based on Ontario registry studies and stroke audits. Age related survival was modeled using Gompertz functions derived from a Canadian population of ischemic stroke survivors. Quality-of-life estimates were taken from stroke survivors in a registry study. Inpatient costs were taken from the Ontario Case Costing Initiative, professional fees from Ontario Schedule of Benefits for Physician Services and other costs from an Ontario cost of stroke study.
Results: In the base case scenario, intravenous thrombolysis resulted in higher functional independence (RR=1.10; 95%CI=1.01-1.20) and similar mortality (RR=0.99; 95%CI=0.74-1.33) to best medical treatment. Compared to best medical treatment, intravenous thrombolysis generated expected incremental QALYs of 0.02 while the expected incremental cost was $1,986. The resulting cost-effectiveness ratio was $115,671/QALY. There was considerable decision uncertainty, driven by clinical uncertainty, which was persistent across all willingness-to-pay. Below a willingness-to-pay of $110,000/QALY, best medical treatment was more likely to be the cost-effective treatment.
Conclusions: Intravenous thrombolysis in late-presentation stroke patients may not be a cost-effective treatment strategy. Future studies of clinical effectiveness are needed to reduce decision uncertainty.
Keywords: *Stroke, cost-effectivness, Ontario*

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Description of drug utilization in newly diagnosed patients with pervasive development disorder in the province of Quebec

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Funding Source: This study was funded through grants received from the Fonds de la recherche en santé du Québec (FRSQ), and the Canadian Institutes of Health Research (CIHR). L. Blais is the recipient of a Salary Award from the *Fonds de la recherché en santé du Québec* (FRSQ) and is the Endowment Pharmaceutical Chair AstraZeneca in Respiratory Health. L. Blais has received research support from AstraZeneca, Amgen, and GlaxoSmithKline.

Background: A number of medication surveys conducted in the U.S. have demonstrated a high level of psychotropic drug usage in patients diagnosed with pervasive development disorder (PDD). Medication use is of interest as not many products are approved for treatment in autism, especially in children.
Objectives: Describe drug utilization in subjects newly diagnosed with PDD in the Quebec province.
Methods: A cohort study was built by using RAMQ and Med-Echo databases for subjects having a new PDD diagnosis (ICD-9 codes: 299.0-299.9) between January 1996 and December 2006. Cohort entry date was the date of a first diagnosis confirmed by the absence of PDD diagnosis in previous 2 years. Descriptive analyses of patient characteristics were done at cohort entry and drug use profiles were done the year prior to, and within the 3 years following diagnosis.
Results: Cohort of 4,373 subjects; 69% male, age: 24.4% (1-5 years), 17.5% (6-13), 7.2% (14-17), 11.4% (18-25), 39.5% (≥26). Prior to being diagnosed with PDD, 53% received psychoactive drugs. Methylphenidate was most common in 6-12 year olds (30.5%) whereas antipsychotics were most common in the 13-17 group (29.8%) and adult population (55%). Antipsychotic use was also present in younger children: 8.1% in 0-5 year olds and 25.2% in 6-12 year olds, 1 year after diagnosis. Antipsychotic, antidepressant and anticonvulsant usage increased in the 3 years following diagnosis, and also with age.
Conclusion: Prior to PDD diagnosis, more than half of the patients were on psychotropic medications, a practice that continued and increased after diagnosis.
Keywords: *Autism, medication, pervasive development disorders, administrative databases*

7

Development of a questionnaire measuring psychosocial determinants of adherence to oral antidiabetic drug treatment

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Background: Approximately one third of patients stop their antidiabetic drug treatment in the first year. Psychosocial determinants of adherence remain unknown. Our objective was to develop a self-administered questionnaire measuring potential psychosocial determinants of adherence to oral antidiabetic drug treatment and assess its psychometric properties.
Methods: The questionnaire was designed using the theory of planned behaviour and constructs from the health action process approach. Constructs measured were: intention, attitude, behavioural beliefs, subjective norms, normative beliefs, perceived behavioural control, self-efficacy, facilitating factors, action planning, coping planning, risk perception, action control and past behaviour. After six sessions of focus groups discussions with 47 type 2 diabetes patients, a first version of the questionnaire was developed and administered to 13 other patients to check for clarity. Another group of 42 patients were then asked to fill an amended version twice, two weeks apart. Internal consistency and temporal stability of constructs and items of this second version were assessed using Cronbach's alphas and intra-class correlation coefficients (ICC), respectively.
Results: To assess psychosocial determinants, a total of 54 questions were developed. Internal consistency or temporal stability were not satisfactory (Cronbach's alpha or ICC <0.70) for some constructs. Based on these results, constructs and items with the highest psychometric properties were selected to be included in the final version of the questionnaire.
Conclusion: The final version of the questionnaire has good content and face validity, internal consistency and temporal stability. It is currently being used in a study among a larger number of patients.
Keywords: *Questionnaires, medication adherence, type 2 diabetes mellitus*

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Disease Risk Scores (DRS) as a summary confounder method: systematic review and recommendations

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Funding Source: CIHR Training Program in Bridging Scientific Domains for Drug Safety and Effectiveness and Fredrick Banting and Charles Best Canada Graduate Scholarship Doctoral Award

Background: Disease Risk Scores (DRS) are summary confounder scores based on the predicted risk of the disease outcome and may be advantageous when: 1) exposure is rare, and 2) to study effect modification by disease risk.
Methods: We completed a systematic search of MEDLINE (keyword) and Web of Science® (citation and author) to identify all English language articles that applied DRS methods. The number of publications was tabulated by year and type (empirical application, methodological contribution, or review paper). The methods used in empirical applications were summarized overall and by year of publication (<2000, 2000+).
Results: Of 714 unique articles identified, 98 studies were eligible, and 86 were empirical applications. A bimodal distribution in the number of publications was identified, with peaks in 1979 and 1980, and then resurgence in use since 2000. The majority of applications derived DRS using logistic regression (42%), used DRSs as a categorical variable (79%), and were applied in cohort (47%) or case-control (42%) settings. The greatest area of growth was in pharmacoepidemiology, with 46% of applications since 2000 vs. 6% before 2000 related to drug exposures. Few studies examined effect modification by disease risk.
Conclusion: Use of DRS has increased yet remains low. Comparative effectiveness research may benefit from more DRS applications, particularly to examine effect modification by disease risk. More research to support use of DRS in case-control studies is needed. A move towards standardization of terminology may facilitate the identification, application and comprehension of DRS methods.
Keywords: *Confounding, epidemiology, epidemiologic methods, pharmacoepidemiology, propensity score*

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Economic benefit of subcutaneous rapid push versus intravenous immunoglobulin infusion therapy in adult patients with primary immune deficiency

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Background: Immunoglobulin replacement therapy in primary immune deficiencies (PID) patients can be achieved intravenously (IVIG) or subcutaneously (SCIG) with similar efficacy and safety profiles. The objective of this study was to evaluate the economic benefit of the rapid push SCIG compared to IVIG infusion therapy in adult PID patients in the context of a program based at St-Paul's Hospital.
Methods: SCIG and IVIG options were compared in a cost-minimization model focused on direct medical costs for infusion supplies and personnel over three years of treatment. A three-year budget impact model assessed the impact of switching from IVIG to SCIG. Sensitivity analyses were performed to measure the robustness of results for both models.
Results: The cost-minimization model estimated SCIG treatment cost per patient over three years at $1978 compared to $7714 for IVIG, resulting in savings to the healthcare system of $5736, principally due to reduced hospital personnel costs. This figure varied from $5035 to $8739 for different modalities of IVIG therapy. Assuming that 50% of BC patients who received IVIG switched to SCIG, the budget impact model estimated cost savings for the first three years at $1,307,894 or 37% of the personnel and supply budget. These figures varied from $1,148,004 to $2,453,933, or 36% to 42% with different modalities of IVIG therapy. If 75% of BC patients switched to SCIG, these figures reached $1,961,841 or 56% of total budget.
Conclusion: Rapid push SCIG for home-based immunoglobulin replacement therapy results in significant savings to the healthcare system in a Canadian context.
Keywords: *Primary immune deficiencies, cost-minimization, budget impact model*

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Impact of exposure misclassification due to incomplete drug data in observational studies of safety and effectiveness: a cohort study

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Funding Source: None

Background: To measure the effect of non-benefit drug use on observed associations between exposure and outcome, thereby documenting the potential magnitude of biases introduced when exposure status is misclassified from non-benefit drug use.
Methods: Among incident diabetic patients in Saskatchewan, Canada, users of benefit and non-benefit thiazolidinediones (TZDs), clopidogrel, and beta-blockers were identified in 2006 and followed until 2008. Differences in all-cause hospitalization or death between users of benefit and non-benefit drugs were evaluated using multivariable proportional hazards models. Bias was assessed by evaluating bootstrapped differences in risk estimates obtained from analyses containing non-benefit and benefit drug use vs. benefit drugs alone.
Results: We identified 5759 TZD users (28% non-benefit), 1551 clopidogrel users (24% non-benefit), and 351 beta-blocker users (42% non-benefit). Users of benefit drugs were more likely to be hospitalized or die than users of non-benefit TZDs (1515 [36%] vs. 420 [26%]; adjusted hazard ratio [aHR] 1.13, 95% CI 1.01-1.26), but not clopidogrel (642 [54%] vs. 171 [46%]; aHR 1.00, 0.81-1.24) or beta-blockers (126 [62%] vs. 73 [49%]; aHR 1.30, 0.88-1.91). Comparing the analyses with (benefit drugs only) and without (addition of non-benefit drugs) drug exposure misclassification suggested minimal bias was introduced for estimated risk of hospitalization or death for TZD [bootstrapped aHR difference +0.05, 0.02-0.08], clopidogrel [+0.01, -0.04-0.06], or beta-blockers [+0.06, -0.09-0.20].
Conclusions: Exposure misclassification from non-benefit drug use is common. Although patient characteristics and outcomes differed between users of non-benefit and benefit drugs, misclassification of drug exposure did not meaningfully bias estimates of risk in our study.
Keywords: *Bias, misclassification, pharmacoepidemiology, pharmaceutical policy, formularies, cohort*

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Impact of maternal attachment on children development at 1-year of age: results from the OTIS Antidepressants in Pregnancy Study

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Background: A poor mother-child relationship has been associated with chronic health problems and weak psychological and cognitive development in children. Our objective was to evaluate the impact of maternal attachment on the cognitive development of 1-year old children whose mothers were suffering from depression or anxiety.
Methods: The OTIS Antidepressants in Pregnancy Study cohort was used. Women were recruited through 9 North American Teratogen Information Services and at the outpatient obstetric clinic of CHU Ste Justine. To be included, women had to be >18 years old, <15 weeks pregnant, and not using known teratogens. Women were followed throughout pregnancy until 12-months post-partum. Maternal attachment and cognitive development were assessed at 12 months postpartum using the Maternal Attachment Postnatal Questionnaire (MAPQ) and the Ages and Stages Questionnaire (ASQ), respectively. The MAPQ and ASQ were administered over the telephone. Socio-demographic, lifestyle and potential confounding variables were also collecting through telephone interviews. Multivariate logistic regression models were built to assess the association between maternal attachment and cognitive development at 1-year of age.
Results: Overall, 215 women and babies were included in this study. The mean age of women was 32.2 years (SD = 4.0). Adjusting for potential confounders, maternal attachment was significantly decreasing the risk of delay in problem-solving skills at 1-year old (Adjusted OR = 0.87; 95%CI (0.76; 1.00)); no significant delay was noted in communication, motor and personal-social skills.
Conclusion: These results indicate that maternal attachment protects children with regards to cognitive development.
Keywords: *Attachment child development*

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Metformin use and the incidence of colorectal cancer in patients with type 2 diabetes mellitus

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Funding Source: Internal Funding Provided by Dr S. Suissa

Background: Metformin is an oral hypoglycemic agent (OHA) prescribed in patients with type 2 diabetes (T2DM). Laboratory studies have suggested that metformin may have potential anti-tumour effects and decrease colorectal cancer incidence. While observational studies have suggested similar effects, most contained important methodological limitation producing results that need to be confirmed using more rigorous methods. The objective of this study is to assess whether metformin is associated with a decreased incidence of colorectal cancer in patients with T2DM.
Methods: Using the United Kingdom GPRD; a cohort study with a nested case control analysis was conducted investigating colorectal cancer incidence in patients with T2DM. All cases occurring during follow-up of the cohort containing patients with T2DM who had been prescribed at least one OHA between 1988 and 2009 were identified. Controls were randomly selected from the cohort within the risk set and matched on age, sex, calendar year of cohort entry, and duration of follow-up. Primary exposure was ever exposure to metformin prior to the risk set follow-up time. Conditional logistic regression was used to estimate adjusted rate ratios.
Results: The cohort was comprised of 115,578 users of OHAs, including 607 cases of colorectal cancer and 5837 matched controls. Metformin was not associated with a change in the incidence of colorectal cancer (RR: 0.94; 95% CI: 0.7-1.2).
Conclusions: Metformin, regardless of dose was not associated with a decreased colorectal cancer incidence in patients with T2DM. These findings contradict results reported in previous observational studies that did not properly account for time.
Keywords: *Type 2 diabetes, metformin, colorectal cancer*

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Pharmacoeconomic evaluation of 13-Valent Pneumococcal Conjugate and 23-Valent Pneumococcal Polysacharide vaccine in Canadian adults

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Funding Source: Pfizer Canada

Introduction: In Canada, a 13-valent conjugate polysaccharide pneumococcal vaccine (PCV13) has recently been licensed for immunocompetent adults aged 50 years or older, as well as children over the age of 5. Currently, a 23-valent pneumococcal polysaccharide vaccine (PPV23) is recommended for high risk adults and all seniors. The health benefits and economic value of vaccinating Canadian adults with PCV 13 instead of PPV 23 is unknown. Compared to PCV13, PPV 23 covers 11 additional serotypes but may not be as effective for the 12 shared serotypes due to PCV13 being a conjugate vaccine as opposed to a polysaccharide.
Objective: To develop a model that compares the health and economic consequences of PCV13 as compared to PPV23 in Canadian adults aged 50+.
Method: We developed a base simulation model for an entire population of providing PCV13 to children less than 2 years of age and simulating the herd effects to the greater population. Vaccinating adults older than 50 years of age with either PCV13 or PPV23 was then compared to the base model, and the health and economic consequences examined across each scenario. Health impacts included invasive pneumococcal disease and pneumococcal related disease. Invasive disease is caused by Streptococcus Pneumococcal and is clinically presented as: meningitis, bacteremia and invasive pneumonia. Pneumococcal related disease is non invasive and has many different etiologies, the main clinical presentations include: otitis media (in base model for children only), and non-invasive pneumonia. Costs and QALYs were contrasted between the two adult vaccination strategies.
Results: Compared to PPV23, PCV13 was associated with 0.278 more cases of invasive pneumonia, 0.061 more cases of bacteremia, 0.002more cases of meningitis, and 27.997 less cases of pneumococcal related disease per 100,000. Compared to PPV23, the incremental cost effectiveness ratio associated with PCV13 was $10,028 per additional QALY gained.
Conclusions: Compared to PPV23, vaccinating adults with PCV13 is cost effective.
Keywords: *Cost effectiveness, vaccine, economic evaluation*

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Pharmacy-based research network: the perception of community pharmacists

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Funding Source: Reseau quebecois de recherche sur l'usage des medicaments and the Agence de la sante et des services sociaux de Laval

Background: Pharmacy-practice research is essential to evaluate new pharmaceutical services and results are often used to justify and promote advanced practices. However, the recruitment of primary-care pharmacists in such research is often challenging. There is therefore a need to develop strategies to facilitate their involvement. Practice-based research network (PBRN) is often presented as one of these strategies.
Objective: To describe the perception of pharmacists regarding PBRN.
Method: A survey was mailed, using a Dillman's tailored design method, to a random sample of 1250 pharmacists in the area of Montreal. It included two questions related to PBRNs to document their interest to participate in such network and their opinion regarding the kind of services and activities such a network might offer.
Results: 571 (45.7%) pharmacists completed the questionnaire; 58.9% indicated they were "very interested' or "interested" in joining a PBRN, while 41.1% reported little or no interest. The most popular potential services were access to continuing education training programs developed in research projects (75.3%); access to clinical tools developed in research projects (76.4%); information about conferences on pharmacy-practice research (63.7%); and participation in the development of new pharmaceutical practices (55.7%).
Conclusion: These results suggest that the level of interest of community pharmacists for PBRN is sufficient to further evaluate its value as an option to optimize and facilitate pharmacy-practice research.
Keywords: *Practice-based research network, community pharmacist, pharmacy-practice research*

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Relative generic usage and drug expenditures after branded patent expiry: not a quick enough switch

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Background: Generic drugs offer a cheaper alternative to exclusive (patented) and branded (formerly patented) drugs. However, even when generic drugs are available, patients may still be prescribed the more expensive branded equivalents, resulting in foregone savings. The objectives of this study were to characterize generic drug usage and quantify the incremental costs associated with the purchase of branded vs. generic drugs for public and private payers.
Methods: We performed a retrospective quantitative analysis of private and public outpatient pharmacy sales in Ontario from 2000 to 2009. We analyzed the purchasing patterns of all drugs in the proton pump inhibitor (PPI), selective serotonin reuptake inhibitor (SSRI), and angiotensin converting enzyme inhibitor (ACE-I) classes because of their widespread use and availability of equivalent generic molecules.
Results: For the three drug classes in the period under study, the additional cost incurred from purchase of branded vs. generic drugs in Ontario was $406 million: $245 million for PPIs, $91 million for SSRIs and $70 million for ACE-Is. The highest proportion of generic prescriptions was for SSRIs purchased by public drug plans and the lowest proportion was for PPIs purchased by private drug plans.
Conclusions: Despite the availability of cheaper generic alternatives, many branded drugs are still sold. The relative added cost of prescribing branded drugs over generics can be significant, differs by drug class and is usually greater for private buyers than for public. Education and policy changes may be the key to encouraging generic substitution and achieving significant cost savings.
Keywords: *Drug substitution, health care economics and organizations, retrospective cross-sectional analysis*

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Reliability of exposure to vaccine products: Agreement between patients' self-report and medical records in the PGRx database

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Background: Patients' self-reported vaccine exposure (PS) may be subject to memory errors and recall biases, while physicians' medical records (MR) do not capture non-compliance issues. This study compared patients' self-report to medical records for exposure to influenza, 23-valent pneumococcal and human papillomavirus (HPV) vaccines.
Methods: Study subjects between the ages of 14 to 79 were recruited from the PGRx network of 300 general practitioners across France without reference to their diagnoses or prescriptions. Physicians provided all their vaccination prescriptions over the previous two years. Patients' self-reported vaccination was obtained from a structured telephone interview for the same period of time.
Results: Agreement between PS and MR was assessed for 7613 patients for whom both sources of information were available. Agreement was substantial for influenza vaccines (bias and prevalence-adjusted kappa = 0.74), and high for 23-valent pneumococcal vaccines (kappa = 0.98) and HPV vaccines (kappa = 0.92). Residual disagreement was associated with gender, age, occupation and chronic medical conditions in multivariate analyses.
Conclusions: Substantial to high agreement between physicians and patients' report suggest that results of studies relying on either source are reliable. This study provided evidence for the first time that this is also true for vaccines that are given during adolescence.
Keywords: *Pharmacoepidemiology, vaccines, concordance study*

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Survival with adherence to beta-blocker medications in heart failure: the 'unhealthy-adherer' effect?

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Background: Many observational studies have shown that the use of BB medications is associated with lower mortality among patients with HF compared to non-users. However, the burden of death owing to non-adherence has not been examined frequently. Attention to the known bias associated with the 'healthy-adherer' phenomenon is required in studies of this nature.
Objective: The purpose of this study was to quantify the burden of death associated with non-adherence to Beta-Blocker (BB) medications among patients with Heart Failure (HF).
Methods: We identified 1,948 subjects from the administrative databases in Saskatchewan who were discharged alive between 1994 and 2003 with a primary

diagnosis of HF, and received a prescription for BB within 6 months of discharge. We measured adherence using prescription fill frequency from electronic pharmacy records and defined adherence as a fill frequency ≥80%. The hazard of death was evaluated using Cox proportional hazard. RESULTS: Among BB users, non-adherent patients had lower hazard of death in both the unadjusted (HR=0.674; 95%CI 0.577, 0.787) and multivariate-adjusted models (HR=0.645; 95%CI 0.549, 0.758). This strong association persisted among all subgroups examined.

Conclusions: In our analysis, adherence to BB was associated with worse outcome of mortality, and the 'healthy-adherer' phenomenon was not clearly demonstrated as a source of bias. Possible explanations for our findings include: a) The clinical heterogeneity among patients coded with HF leading to a residual confounding; b) higher adherence among more severely afflicted subjects, c) ineffectiveness of BB among certain subgroups of elderly patients with perceived HF syndromes.

Keywords: *Adherence, beta-blockers, heart failure survival*

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Systematic follow-up of fragility fractures: preliminary results of a treatment adherence

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Background: Fragility fractures are under-diagnosed and treated. We are at validating a process of a multidisciplinary systematic follow-up approach for osteoporosis using a clinical nurse. The aim of the study was to evaluate the use of antiresorptive agents after enrollment of the patients in the systematic follow-up.

Methods: We enrolled in the last year 300 subjects over 40 years of age who are treated for a fragility fracture at the Montreal Sacre-Coeur Hospital from July 2010 to 2011. After starting a treatment protocol for osteoporosis, they are followed for a 24-months period. They have to complete questionnaires, medical exams and be evaluated on their compliance to treatment. We reconstructed the exposure to preventive medication by using pharmacy claims and the prescription refills in a subset of the cohort.

Results: Among 74 women and 16 men, the average age was 59.7 years. The most common fractures were wrists (n=42). The average femoral BMD was -1.52 and -1.72 for the vertebra. The pharmaceutical follow-up showed that 12,6% patients were already on antiresorptive agents and 90% of the patients received at least one dispensation after their fractures. About 67% fulfilled their prescriptions in the first week, where only 55.6% were under tritherapy (bisphosphonates, calcium and vitamin D). This rate declined to 32.1% after the third refill.

Conclusion: Preliminary results show that the adherence decreases strongly after the first three months. We expect to improve the adherence to antiresorptive agents by having access to pharmaceutical files in real time during the systematic follow-up.

Keywords: *Osteoporosis, adherence, antiresorptive agents*

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The effect of treatment adherence on smoking abstinence in patients post-acute myocardial infarction

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Background: Previous trials examining the use of bupropion as a smoking cessation therapy in post-acute myocardial infarction (AMI) patients have been inconclusive. These findings may be explained, in part, by adherence to study medication.

Methods: We used data from a randomized, double-blind, placebo-controlled trial of bupropion in smokers (N=392) hospitalized with AMI to determine the effect of treatment adherence on abstinence. Adherence was assessed by self-report throughout the 9-week treatment period. Patients were classified as adherent if they reported taking 2 pills/day at each follow-up. Abstinence was assessed by 7-day biochemically-validated self-report at 9 weeks (n=385), 6 months (n=380), and 1 year (n=377). Patients lost to follow-up were considered to be non-adherent and to have returned to smoking.

Results: Patients were predominantly male (83.3%), and the mean age was 53.8 years (SD 10.4). Patients who were adherent to treatment (bupropion or placebo) at 1 year reported greater abstinence than those who were not (52.3% vs. 35.6%). In patients who were adherent, the prevalence of smoking abstinence at 1 year

was similar in the two treatment groups (52.3% and 48.9%, respectively). Conversely, among those who were not adherent, randomization to bupropion resulted in a substantial increase in abstinence [Difference (Bupropion - Placebo) = 13.0, 95% CI: 1.2, 24.7]. A similar difference was observed at 6 months.
Conclusions: Adherence to study medication, regardless of assigned treatment, is associated with substantial increases in abstinence. Post-AMI patients with lower levels of motivation may derive greater benefit from the use of bupropion for smoking cessation.
Keywords: *Smoking abstinence, bupropion, treatment adherence, acute myocardial infarction*

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The efficacy and safety of new oral anticoagulants versus warfarin in patients with atrial fibrillation: a systematic review and meta-analysis

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Background: New oral anticoagulants, including apixaban, dabigatran, and rivaroxaban, have been developed as alternatives to warfarin, the standard oral anticoagulation therapy for patients with atrial fibrillation (AF). We performed a systematic review and meta-analysis of randomized controlled trials (RCTs) to compare the efficacy and safety of new oral anticoagulants to warfarin in patients with AF.
Methods: We systematically searched the literature for RCTs of more than 1-year duration that compared new oral anticoagulants to warfarin in patients with AF. Random-effects models were used to pool efficacy and safety data across RCTs.
Results: Three studies, including 44,563 patients, were identified. Patients randomized to a new oral anticoagulant had a decreased risk of all-cause stroke and systemic embolism (RR [relative risk], 0.78; 95% confidence interval [CI], 0.67, 0.92), ischemic and unidentified stroke (RR, 0.87; 95% CI, 0.77, 0.99), hemorrhagic stroke (RR, 0.45; 95% CI, 0.31, 0.68), all-cause mortality (RR, 0.88; 95% CI, 0.82, 0.95), and vascular mortality (RR, 0.87; 95% CI, 0.77, 0.98). Randomization to a new oral anticoagulant was associated with a lower risk of intracranial bleeding (RR, 0.49; 95% CI, 0.36, 0.66). Data regarding the risks of major bleeding (RR, 0.88; 95% CI, 0.71, 1.09) and gastro-intestinal bleeding (RR, 1.25; 95% CI, 0.91, 1.72) were inconclusive.
Conclusion: The new oral anticoagulants are more efficacious than warfarin for the prevention of stroke and systemic embolism in patients with AF. With a decreased risk of intracranial bleeding, they appear to have a favorable safety profile, making them promising alternatives to warfarin.
Keywords: *Oral anticoagulation, atrial fibrillation, meta-analysis*

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The impact of the type of drug insurance plan on costs of antidepressants and statins

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Background: The impact of the type of drug insurance plan on costs of medications is not well known. We aimed to compare the costs of antidepressants and statins, two of the most prescribed drugs, in Quebec patients who are covered by private and public drug insurance.
Methods: Two matched cohort studies were conducted using prescription claims databases for Quebec residents with private (reMed) and public drug insurance (RAMQ). Patients were aged 18 to 64 years and filled at least one prescription for an antidepressant (Cohort 1) or a statin (Cohort 2) in monotherapy between December 2007 and September 2009. The average monthly costs (medication cost + dispensing fee) of antidepressants and statins per patient and the percent cost difference for a 30-day prescription for each antidepressant and each statin product were compared between patients with private and public drug insurance using t-tests.
Results: Cohort 1 included 194 privately and 1923 publicly insured patients while the corresponding figures for Cohort 2 were 174 and 1712, respectively. The average cost of antidepressants and statins per patient per month was significantly higher among privately-insured than publicly-insured patients [Cohort 1: 48.17±25.19$ vs. 33.72±17.58$, p<0.001; Cohort 2: 61.19±22.31$ vs. 54.62±20.48$, p<0.001]. The cost of 30-day prescriptions for most individual drugs of antidepressants and statins was significantly more expensive for privately-insured patients than publicly-insured patients.

Conclusions: Higher cost of antidepressants and statins observed in privately-insured patients might be due to different pharmacy payment requirements and the dispensing fee restrictions under the public plan.
Keywords: *Drug insurance plan, costs, antipressants, statins*

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Treatment with rivastigmine or galantamine and hospitalization for an adverse cardiac event: a Dutch database study

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Funding Source: The study received financial support from the Canadian Institutes for Health Research (CIHR) (Research Fellowship for E. Kröger), from the division of Pharmacoepidemiology and Pharmacotherapy at Utrecht University (UIPS) and the Centre d'excellence sur le vieillissement de Québec (CEVQ). The division of Pharmacoepidemiology and Pharmacotherapy at Utrecht University, which employs T. Egberts and P. Souverein, has received unrestricted funding for pharmacoepidemiological research from GlaxoSmithKline, Novo Nordisk, the private-public funded Top Institute Pharma, the Dutch Medicines Evaluation Board and the Dutch Ministry of Health.

Background: Two Cholinesterase inhibitors (ChEIs), rivastigmine and galantamine, for which adverse cardiac events have been reported, are used to treat Alzheimer Disease in the Netherlands. This study assessed whether their use increased the risk of cardiac events in this country.
Methods: A cohort-crossover study of the PHARMO Record Linking System database included patients who initiated ChEIs at age 50+, had at least one ChEI dispensing between 1998 and 2008, a one year history in PHARMO and one subsequent dispensing of any medication. The outcome was a first hospitalization for syncope, AV block, heart failure (HF), dysrhythmia, ischemic heart disease (IHD) or myocardial infarction (MI). Poisson and Cox regression were used to calculate incidence densities and hazard ratios (HR) for cardiac events during periods with, as compared to periods without, ChEI use.
Results: During the observation period of 8.9 years (IQR: 6.7; 10.2) there were 569 cardiac events among 3358 patients. The adjusted incidence densities (ID) were significantly increased during ChEI exposure for syncope, AV-block, HF and MI, when compared to the background ID, in the years prior to the last year before ChEI initiation. However, when exposed periods were compared to the unexposed periods of one year before ChEI initiation and times after exposure, the adjusted HRs were not significantly increased for syncope, AV-block, HF, dysrhythmia or MI. The adjusted HR for IHD was 1.91 (95% CI 1.00-3.67).
Conclusion: Exposure to ChEIs might increase adverse cardiac events, but the small numbers of cases limits conclusions about risk in this population.
Keywords: *Cholinesterase inhibitors, Alzheimer's disease, cardiac events, administrative database, adverse events*

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Trends in post-traumatic use of analgesics and arthritic-related medications following lower-limb joint injuries in the population of the province of Quebec, Canada

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Background: Trends in post-traumatic use of analgesics and arthritic-related medications are lacking. The aim of this study was to determine the proportions of individuals who filled analgesics and arthritic-related drug claims following lower-limb joint injuries in the province of Quebec, Canada.
Methods: This was a population-based observational study. Quebec residents who had a fracture or dislocation of a lower-limb joint between 1998 and 2002 were identified from the Quebec Trauma Registry. The pharmaceutical services of the individuals covered by the Quebec public drug regimen were reviewed to determine the yearly proportions of individuals who filled analgesics and arthritic-related drug claims during a five-year post-injury follow-up.
Results: There were 5106 (87.0%), 3645 (77.6%), 2445 (76.4%), 1601 (76.3%) and 879 (73.0%) individuals with ≥ 1 analgesic or arthritic-related drug claim in the five years post-injury. The proportion of individuals with ≥ 1 paracetamol claim decreased from 41.9% in the first year to 25.3% in the fifth year. The proportions of individuals with ≥ 1 claim of acetylsalicyclic acid and PPIs increased from 30.2% and 22.9% in the first year to 38.1% and 32.1% in the fifth year, respectively. Opioids were used by 49.0% of the individuals in the first year and by 19.0% in the next four years. In the

fifth year, DMARDs, glucocorticosteroids, NSAIDs, calcium and vitamin D were used by 2.4%, 8.5%, 28.4%, 29.6% and 18.0% of the individuals, respectively.
Conclusions: The majority of the individuals are using analgesics and arthritis-related medications during the five years following lower-limb joint injuries.
Keywords: *Post-traumatic arthritis, drug utilization, governmental drug claims administrative database*

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Variation in the days supply field for osteoporosis medications in Ontario

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Background: Pharmacy claims data are commonly used to examine patterns of drug utilization and to classify drug exposure in post marketing surveillance. However, the accuracy of the days supply field has not received great attention.
Methods: We used data submitted to the Ontario Drug Benefits program (ages 65+ years) to examine the variation in days supply reported for osteoporosis medications, 1997-2011. The number and proportion of days supply values submitted were summarized by dosing regimen and residence status (community or long-term care [LTC] resident).
Results: We identified 17,615,364 osteoporosis prescriptions dispensed to community (78%) or LTC (22%). Most daily oral prescriptions (97%) were dispensed in 7- or 30-day intervals, or as 100 days supply. However, distinct differences were observed for other regimens, with the typically expected days supply more common in community vs. LTC: cyclical etidronate (90-day supply; 86% vs. 40%), weekly oral regimen (7- or 30-day intervals; 91% vs. 60%), and monthly oral regimen (94% vs. 35%) or nasal spray (84% vs. 40%) dispensed in 28- or 30-day intervals. In both settings, annual zoledronic acid infusion was most commonly dispensed as 1 day supply (62%).
Conclusions: Results suggest that there may be significant reporting errors in the days supply field in Ontario pharmacy claims, particularly among prescriptions dispensed in LTC. The variation noted for osteoporosis medications in Ontario are likely indicative of similar reporting errors for other drugs and in other regions. Errors in the days supply field may have significant implications for drug exposure misclassification in pharmacoepidemiologic studies.
Keywords: *Pharmacy claims, osteoporosis, days supply*

POSTER PRESENTATIONS

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A novel knowledge translation approach for addressing the role of obesity in prescribing practices

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Background: We studied the association between obesity, prescribing practices and increased risk of antibiotic treatment failure (ATF). Of the 6179 study patients prescribed antibiotics, 13.4% suffered ATF. After adjusting for other potential confounders, obesity was a significant predictor of ATF (OR 1.26; 95% CI 1.03-1.52). We concluded that this association was likely due to not adjusting dose for weight. As obesity remains a difficult topic of conversation in the context of clinical visit, we are proposing a novel strategy for knowledge translation for key stakeholders.
Methods: Research suggests that controversial scientific developments should be made the topic of public debates to maximize benefit and appropriateness of dissemination. Techniques employed to engage key participants are diverse and include deliberative consultations, providing a framework for decision-making where the impact of research is placed within a frame of socially agreed practices. We will be holding a series of consultations to determine optimal strategies to address obesity and prescribing in primary care for relevant participants: healthcare providers, patients and health care stakeholders. Participants will be asked to deliberate on the conclusions of our research (i.e. lack of weight based dosing, how to address this, etc). The conversational exchange within the consultations will be analyzed using thematic textual analysis.
Conclusions: We expect to identify critical themes with policy development recommendations. Our previous experience holding deliberations on the topic of pharmacgenomics indicate that there is widespread agreement among participants that deliberations result in subsequent health policy development that is accountable and transparent to the public.
Keywords: *Prescribing practices, obesity, knowledge translation*

ENCORE PRESENTATION

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Administrative data in rheumatology research and surveillance: best practices

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Funding Source: Canadian Arthritis Network

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AGIR: A self-management program for osteoarthritis patients and primary care clinicians supported by a group of interdisciplinary regional clinicians

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Funding Source: Institutes in partnership with AstraZeneca. Pfizer Canada Inc. also funded a part of the project.

Background: As part of a knowledge translation program, a one-day workshop was conducted to explore the perception of primary care (PC) actors regarding changes that could be implemented to provide better care to patients with chronic non-cancer pain. Priorities for action included the provision of interprofessional continuing education program and the improvement of patient's self-management.
Objective: Translate those priorities for action into a PC program.
Methods: Over a eight month-period, members of the PC community (physiotherapist, pharmacist, nurses, PC physicians, anaesthesiologist, and researchers) worked together to define the target population and the components of the program and to develop the program.
Results: Patients with osteoarthritis were selected as the target population. The program is entirely supported by a group of interdisciplinary regional clinicians. It includes a self-management program for patients and their family. Over a two session-period, patients will define their objectives and treatment plan (lifestyle changes and medications). A one session interactive interdisciplinary training program will be offered to PC physicians, nurses, pharmacists, and physiotherapists. They will learn about pain management and interdisciplinary collaboration. Pharmacists will also attend a short training session on medication review process and will be invited to meet each patient individually. Finally, PC physicians will have access to pain specialists through a weekly telephone consultation service.
Conclusions: AGIR program was developed by PC actors in accordance with the chronic care model. A pilot clinical trial will be initiated to assess its feasibility and potential effectiveness.
Keywords: *Osteoarthritis, education, primary care*

ENCORE PRESENTATION

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An application of a proposed framework for formulary listing in low-income countries: The case of Cote d'Ivoire

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Antimalarial drugs and the risk for the pregnant women and fetuses: review of the literature

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Background: WHO recommends the use of artemisinin combination based therapies (ACT) and quinine +clindamycin for the treatment of malaria in pregnancy. Pregnant women are inadvertently exposed to all

antimalarials during gestation. Very little is known about the safety of these drugs during this period.
Objective: This literature aims to provide an update on the risks associated with gestational use of antimalarial during pregnancy.
Methods: A systematic search in PubMed was performed using the following keywords: ("antimalarial" [MeSH Terms] OR "Antimalarials" [All Fields] OR "Antimalarials" [Pharmacological Action]) AND ("pregnancy" [MeSH Terms] OR "pregnancy" [All Fields])) AND ("Human" [MeSH Terms] AND ("1966/01/01" [PDAT]: "2012/04/30" [PDAT])). Other than having a comparative study, there were no other exclusion criteria. A systematic review was performed on all studies identified.
Results: The literature review identified 70 studies. The majority were on antifolates (31.4%), and artemisinin combination therapies (17.14%). Data on quinine use during pregnancy are reassuring. The risk of mefloquine during the 1st trimester of pregnancy is controversial. To date there is no evidence on the safety of amodiaquine in pregnancy in the literature. Antifolates as a group reported an increased risk of birth defects (RR= 3.4; 95% CI, 1.8 to 6.4) during the second and third trimester of pregnancy. The safety of artemisinin and its derivatives is not yet clearly established.
Conclusions: The risk of antimalarials in pregnancy, mainly in the first trimester of pregnancy, is not widely reported in the literature. However, antifolates should clearly be avoided.
Keywords: *Safety, antimalarials, pregnancy, risks*

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Antipsychotic use in elderly patients with dementia in Quebec, in 2006 and 2009

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Funding Source: none

Background: Seniors with dementia who present neurobehavioural disturbances and need antipsychotic treatment are at a higher dose-dependent risk for mortality and cerebrovascular events. Health Canada issued three warnings to health care professionals to limit antipsychotic use.
Methods: We conducted a retrospective cross-sectional study in people with dementia aged 65 and over who were covered by the RAMQ*-managed Public Prescription Drug Insurance Plan in 2006 and 2009. Information regarding the antipsychotics administered, as well as socio-demographic and medical information (medical services, diagnostic codes) for these patients was obtained from RAMQ computer files. A descriptive analysis was performed on this population, based on antipsychotic use, type of therapy, duration, doses (low, moderate, high, and associated with a high risk of mortality) and follow-up.
Results: Antipsychotic use increased by 13.3% between 2006 and 2009 in seniors with dementia. The most prescribed antipsychotic was risperidone. High doses were prescribed in 8.3% of cases, and doses associated with a high mortality risk in 25.2% of cases. Follow-up was mostly performed by family physicians; however, 25% of patients in 2006 and 15% in 2009 were not subject to any follow-up in the 365 days following the prescription of antipsychotics.
Conclusion: Antipsychotic use has increased in seniors with dementia, despite warnings issued by Health Canada. The use of high doses and of doses associated with a high risk of mortality without sufficient evidence base gives cause for concern and highlights the need for drafting guidelines on the use of antipsychotics in this population.
Keywords: *Antipsychotics, elderly, mortality, dementia*

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Caffeine intake during pregnancy and the risk of preterm birth

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Background: Given that pregnant women commonly consume caffeinated beverages, caffeine intake during pregnancy has been the subject of many epidemiological studies regarding its potential reproductive adverse effects on the foetus. The risk for preterm birth is one of the most studied outcomes in animal studies.
Objective: To quantify the association between caffeine intake during pregnancy and the risk of preterm birth.
Methods: A questionnaire was mailed to 8505 women randomly selected from the Quebec Pregnancy Registry which was created with the linkage of three administrative databases: RAMQ, MED-ECHO, and ISQ. Eligible women gave birth to a singleton liveborn between January 1998 and December 2003 in Quebec and were insured by the RAMQ drug plan for at least 12 months before and during pregnancy. Questionnaire data were linked to the Registry data and responders constituted the study population. Prematurity was defined as a delivery occurring before 37 weeks of gestation; the remaining was defined as term pregnancy. Descriptive statistics and multivariate logistic regression models were used to analyze data.

Resuts: 3354 (40.6%) responded to the questionnaire. In order to have a representative sample of the registry, only 7% of birth defects cases were selected. Given that, our present study included 1648 pregnancies. Among them 506 (30.7%) cases of prematurity were identified. Adjusting for potential confounders, caffeine intake during pregnancy was not associated with the risk of prematurity [OR=0.96, 95% CI (0.72-1.28)].
Conclusion: Caffeine intake during pregnancy does not significantly increase the risk of prematurity.
Keywords: *Caffeine pregnancy, prematurity*

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Changing scientific and policy paradigms in the pharmaceutical sector: reflections from a program of research conducted in partnership with decision makers

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Background: We studied the relationships between global trends in the drugs development and challenges faced by pharmaceutical policy makers in Canada and abroad.
Methods: Using US FDA datasets, we identified trends in the number and nature of drugs developed since 1945. Drugs were classified by therapeutic class (WHO ATCs) and by therapeutic novelty (first-in-class, early follow-on, and late follow-on drugs). Policy trends were identified through four research studies involving persons responsible for pharmaceutical licensing, assessment, and funding from 11 countries. Transcripts from telephone interviews and focus groups were analyzed using thematic coding structures.
Results: Although total drug discoveries are currently at a 30-year low, the average number of first-of-kind discoveries has not fallen below historical averages. Continued pioneering discoveries are being made in specialized medicine categories. Policy trends mirror this. Active, evidence-based formulary management helped to manage blockbuster drug classes in the 1990s but the transition to "nichebusters" places new challenges on evidence-based decision-making paradigms. A common policy response is increased reliance on post-market evaluation.
Conclusion: Policy development in the pharmaceutical sector is influenced by trends in both the number and nature of drugs being discovered. In the emerging era of specialized medicine, policymakers will need to work together - both across Canada and internationally - to advance the standards and transparency of evidence used to address these challenges.
Keywords: *Scientific paradigms, policy paradigms, pharmaceutical policy making, comparative policy analysis*

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Comparative analysis of interprovincial and international legal framework and modalities for negotiations between public payers and pharmaceutical manufacturers on price and reimbursement of drug products - Proposal of a conceptual framework for Quebec

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Background: The managers of drug plan are facing situations where they have to make reimbursement decision based on pharmacoeconomic and clinical data that are either sparse or bared on limited number of patients or clinical trials. In these cases, a favorable reimbursement decision is often impossible because of the potential clinical and/or economic uncertainty associated with a drug product, hence limiting patient access to potential beneficial therapy. Quebec has a regulatory framework to enable the negotiation of agreements to share financial risk with drug manufacturers. The implementation seems complex. The negotiation of such agreements in clearly defined situations, however, constitutes an interesting approach offering benefits for patients, government and manufacturers: faster access to innovative treatments, management of clinical and/or economic uncertainty associated with a pharmaceutical product and access to market faster for manufacturers.
Results: This project, based on a comparative analysis of the regulatory environment concerning the reimbursement and drug price for selected Canadian provinces as well as for UK, proposes a conceptual framework for the implementation of such agreements. The agreements, to be optimal, will have to take into account the incentives for each participants as well as the importance of the transparency of information, the integration of the process to evaluate, negotiate and monitor the agreements and, finally, the availability of expertise and management mechanisms.
Conclusion: The implementation of the proposed conceptual framework could be an interesting approach to manage new products and should require little or no legal changes depending on the selected applications modalities.
Keywords: *Risk-sharing agreement, reimbursement, pharmaceutical*

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Cost-effectiveness of TOCTINO® (Alitretinoin) versus cyclosporine in adult patients with severe chronic hand eczema unresponsive to potent topical corticosteroids

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Background: Severe chronic hand eczema (CHE) is associated with a significant burden to patients and the society; contributing to sick leave and compensation for time off work. The BACH study demonstrated that patients significantly benefited from treatment with TOCTINO® (alitretinoin). The objective of this analysis was to determine the cost-effectiveness of TOCTINO compared to cyclosporine in adults with severe CHE unresponsive to potent topical corticosteroids.
Methods: A Markov model was developed that captures time spent by patients in various health states, as defined using the patients' PGA status: Clear/Almost Clear (responders), Mild/Moderate (non-responders) and Severe (non-responders). Results were reported as incremental costs per additional quality adjusted life-years (QALY) gained, over a 12-year period. Transition probabilities were derived from the BACH study for TOCTINO and the published literature for cyclosporine. Utilities were derived from a mapping study converting the PGA to the EQ-5D. Cost data were obtained from a variety of sources and reported as 2011 Canadian Dollars. Multiple sensitivity analyses were undertaken to test the robustness of the model.
Results: From the public healthcare perspective, TOCTINO is cost-effective compared to cyclosporine with an incremental cost-utility ratio (ICUR) of $15,452 per additional QALY gained. From the societal perspective TOCTINO is dominant to cyclosporine (i.e., TOCTINO is more effective and less costly). Results were robust over a wide range of sensitivity analyses tested.
Conclusions: TOCTINO is a cost-effective treatment for adult patients with severe CHE unresponsive to potent topical corticosteroids relative to cyclosporine.
Keywords: *Cost utility analysis, alitretinoin, chronic hand eczema*

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Costs of moderate to severe pain in primary care patients - A study of the Programme ACCORD

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Funding Source: This study was funded by a team grant - Community Alliances for Health Research and Knowledge Exchange in Pain of the Canadian Institutes of Health Research (CIHR) in partnership with AstraZeneca Canada Inc (Grant # 86787), and by Pfizer Canada Inc.

Background: In Canada, more than 3.9 million of individuals suffer of CNCP, a disorder that is associated with low quality of life and that represents substantial economic burden to societies, burden that remains however insufficiently documented.
Objective: This study evaluates the annual direct and productivity costs associated with CNCP in primary care in function of pain severity and functional disability.
Methods: Patients recruited in primary care, reporting non-cancer pain for at least 6 months, at a pain intensity of more than 4 on a 0 (no pain) to 10 (worst possible pain) scale and at a frequency of at least 2 times et week. A cohort study conducted in Québec (Canada). Information on healthcare resources utilization and on pharmacotherapy was retrieved from the RAMQ database, from the MedEcho database, as well as from pharmacies' renewal charts. Pain characteristics, productivity losses, over-the-counter medications and complementary healthcare services utilization were documented from a telephone questionnaire.
Results: 486 patients participated. They were on average 58.4 years old, were mainly women (67.7%) and suffered of non-cancer pain for a mean of 11.7 years at an average pain intensity of 6.5. Mean annual direct costs per individual vary between 5690.28$ (8046.17$) and 9564.70$ (11 497.19$), increasing with higher level of pain severity and functional impairment. Mean annual productivity costs represented 3539.30$ (10 187.53$) and the mean annual total costs amounted 11 359.88$ (16 316.30$).
Keywords: *Chronic non-cancer pain, direct costs, productivity costs*

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Development of a new tool to evaluate the severity of drug-related problems in chronic kidney disease patients

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Funding Source: Instituts de Recherche en Sante du Canada

Background: The quality of medication use in chronic kidney disease (CKD) patients is not always optimal with a mean of 3.5 drug-related problems (DRPs) per patient. However, no information is available regarding their severity.
Objective: To develop a set of criteria to evaluate the severity of DRPs in CKD patients from a community pharmacy perspective.
Methods: The Schneider criteria were initially adapted by a team of clinicians and researchers to take into account the type of community pharmacists interventions required to manage DRPs at each level of severity. Thereafter, ten community pharmacists were consulted individually. Finally, the relevance of each criterion was first individually rated by 12 experts on a scale from 1 (not relevant) to 4 (relevant). Thereafter, in a consensus meeting, criteria initially judged as irrelevant by more than 20% of experts were discussed.
Results: Three levels of severity (mild, moderate and severe) were defined and each level is further categorized in two sub-levels. For each level and sub-level, the specific pharmaceutical interventions required to manage DRPs were listed. These include the provision of information to patients, the application of a collective prescription, the monitoring of physiologic parameters (e.g. blood pressure or glycemia), the adaptation of a prescription, the writing of a pharmaceutical opinion, and the referral of patients to their primary care physician or to the emergency department.
Conclusion: The psychometric properties of these criteria will now be evaluated. If satisfactory, these criteria will constitute a new tool for pharmacy practice researchers.
Keywords: *Drug-related problems, chronic kidney disease*

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Disparities in access to cancer drugs as a result of provincial government pharmaceutical policies

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Funding Source: None

Background: Provincial pharmaceutical policies vary greatly, even more so when it comes to cancer drugs. province provides funding of cancer drugs to its residents through different publicly funded drug programs. The purpose of this study was to examine how these policies translate into disparities in access to cancer drugs across Canada.
Methods: Data was extracted from the Cancer Therapy Navigator database to examine the extent of public drug plan funding disparities for cancer drugs as a result of different provincial pharmaceutical policies. Funding in each province was segmented into seven coverage categories. Fifty cancer drugs approved since 1995 were examined. Each drug's highest level of funding was reported based on any indication funded.
Results: The level of access to cancer drugs is greatest in British Columbia (38/50), followed by Quebec (37/50), Saskatchewan (32/50), Nova Scotia (32/50) and Alberta (31/50). Pharmaceutical policies in British Columbia, Alberta and Saskatchewan are most similar, however, British Columbia has more drugs funded under case-by-case criteria than Alberta and Saskatchewan. Cancer drug funding in Manitoba and Ontario is shared among the respective cancer agency's formulary and the general public drug formulary. Access to cancer drugs is lowest in New Brunswick, Prince Edward Island and Newfoundland where pharmaceutical policies vary by cancer treatment centers and are not directed at the provincial funding level.
Conclusions: Provincial pharmaceutical policies have resulted in disparities in the level of access to cancer drugs across Canada. Funding is available through a number of publicly funded drug programs, which makes patient navigation difficult.
Keywords: *Cancer, access, policy, funding*

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Epidemiology of major congenital malformations with specific focus on teratogens

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Background: Major congenital malformations (MCM) are significant causes of infant morbidity and mortality and constitute important societal and economic burden.
Methods: We conducted a literature review to synthesize current evidence on MCM. Specific objectives were to: 1) summarize internationally reported prevalence of MCMs based on registries and surveillance systems; 2) describe the epidemiology of different MCM types including critical periods,

causative factors; 3) to identify the role played by principal known teratogens on the increase in the risk of MCM; and 4) determine challenges associated with the epidemiologic assessment of potential risk factors for MCMs as well as potential preventive measures.
Results: It is estimated that 7.9 million infants worldwide are born every year with a MCM, yet there is considerable variation in reported rates across countries. This may be attributable to varying definitions arising from heterogeneity among different classes with respect to critical periods for embryogenesis and organogenesis. There is also substantial etiologic heterogeneity among MCM classes that potentially contribute to challenges in epidemiologic studies. Modifiable factors such as pharmacologic exposures have received considerable attention and a number of drugs have been shown to be teratogenic including folic acid antagonists, angiotensin converting enzyme inhibitors, antidepressants, anticonvulsants, coumarin derivatives and retinoids including isotretinoin.
Conclusion: The majority of MCM are due to unexplained causes; other contributing factors include genetics, multifactorial inheritance, environmental factors, maternal-related conditions, and maternal drug or chemical exposure. However, there remains a need to better understand the epidemiology of MCM when studying drug effect during gestation.
Keywords: *Epidemiologic review, major congenital malformations, teratogens*

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Fat consumption in first and fourth year university students

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Background: Poor diets can lead to increased risk of health problems, such as cardiovascular disease, diabetes and hypertension, in the general population. Studies have suggested that university students consumed diets that are high in fats and saturated fats. Previous studies compared the consumption of fat in first and fourth year science students at St. Francis Xavier University . They found that not only did fourth year students consume less total and saturated fat than first year students, but students who have taken a nutrition course consume less total and saturated fat than those who have not. However, this was only seen in science courses. The purpose of this study is to compare fat and saturated fat consumption among arts and science students in first and fourth year university courses, and see whether taking a nutrition course would improve fat consumption.
Methods: A sample of first year and fourth years, in both arts and science students, will be used. They will complete a survey using a demographic questionnaire designed by the research and a food frequency designed by Dr. Gladys Block. Data will be analyzed using algorithms derived from Dr. Blocks study to determine total fat, saturated fat, percent fat and total cholesterol intake. We will then make statistical inference using Statistical Packages for the Social Sciences (SPSS) 2012 and use independent sample T-tests and Chi square tests.
Results: The study will be complete in March 2012
Conclusions: The findings of this study will help inform health professionals as to whether interventions aimed at increasing nutrition knowledge are worth exploring as a strategy to decrease total fat and saturated fat consumption in university students.
Keywords: *Nutrition knowledge, fat consumption, students*

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Fluoroquinolone therapy and idiosyncratic acute liver injury: a population-based study

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Background: Although fluoroquinolones are occasionally associated with mild, transient aminotransferase elevation, serious acute liver injury (ALI) is rare. Regulatory warnings have identified moxifloxacin as presenting a particular risk of ALI. We examined the risk of idiosyncratic ALI associated with moxifloxacin relative to other selected antibiotics.
Methods: We conducted a population-based, nested case-control study of Ontario health care data from April 2002 to March 2009. Cases were outpatients aged 66 years and older with no history of liver disease who were hospitalized for ALI within 30 days of a prescription for one of five broad-spectrum antibiotics: moxifloxacin, levofloxacin, ciprofloxacin, cefuroxime or clarithromycin. For each case we selected up to 5 age/sex-matched controls who received a study antibiotic, but who were not hospitalized for ALI. Odds

ratios were computed for the association between hospitalization for ALI and prior antibiotic exposure, using clarithromycin as the reference.
Results: 121 patients were hospitalized for ALI within 30 days of antibiotic prescription, 73 (60.3%) of whom died during the index hospitalization. After multivariable adjustment, use of either moxifloxacin or levofloxacin was associated with a two-fold risk of ALI relative to clarithromycin (adjusted odds ratios 2.02, 95 percent confidence interval 1.02 to 4.01; and 2.14, 95 percent confidence interval 1.04 to 4.42, respectively). No such risk was observed with either ciprofloxacin or cefuroxime.
Conclusions: Among older outpatients without evidence of liver disease, moxifloxacin and levofloxacin were associated with an increased risk of ALI relative to clarithromycin. Regulatory warnings regarding fluoroquinolone-associated ALI should include both moxifloxacin and levofloxacin.
Keywords: *Fluoroquinolone, moxifloxacin, hepatotoxicity*

ENCORE PRESENTATION

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Glucocorticoid therapy and serious infections in rheumatoid arthritis: a nested case-control study using a weighted cumulative dose model

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Growing prescription drug costs, despite more efficient health care delivery, in cases with systemic autoimmune rheumatic diseases in British Columbia, Canada: a population-based study

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Background: We estimated the unknown health care burden of SARDs (systemic lupus erythematosus, systemic sclerosis, Sjögren's disease, poly/dermatomyositis, and systemic vasculitis) at the population-level and, for the first time, longitudinally.
Methods: Using a previously-defined algorithm, we established a population-based cohort of SARDs cases. Our administrative data captured all provincially-funded outpatient services and hospitalizations consumed from 1996-2007, and all dispensed prescriptions. Outpatient and prescription costs were summed directly from paid claims; case-mix methodology was used for hospitalizations. Costs are reported in 2007 Canadian dollars.
Results: We identified 18,741 SARD cases, contributing 82,140 patient-years (PY). After inflation adjustments, annual overall mean per-PY costs decreased by 20% over 12-years, from $8901-$7123/PY. Outpatient encounters and costs decreased: by 19% (34-27/PY) and 26% ($2205-$1641/PY), respectively. Mean annual hospital costs decreased by half (from $5579-$2776/PY) and admissions by 46% (0.89-0.48/PY) over 12-years. Despite these decreases, the annual mean number of dispensed prescriptions increased by 49% (23-34/PY) and their costs by 50%, from $1117-$1670/PY. Newest SARDs therapies during the study period (Rituxan and CellCept) were responsible for only 4% of drug costs in 2007, suggesting complications or comorbidities may be the main contributors to the increase in medication costs.
Conclusions Long-term reductions in health care costs for SARDs are encouraging and suggestive of more efficient health service delivery. However, medications are the only growing factor (by 4% annually, on-average). As comorbidity burdens rise and demand grows for expensive but potentially-better SARDs therapies, further research to assess the impact of new therapies on comorbidity risk will be needed.
Keywords: *Provincial administrative data, systemic autoimmune rheumatic disease, health economics*

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High cost beneficiaries of the Ontario Drug Benefit (ODB) Program

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Background: Over the past 5 years, Ontario Public Drug Program (OPDP) expenditures have grown by 8%, and analyses have shown that a small percentage of beneficiaries account for a disproportionate share of program expenditures. Together, the Ontario Drug Policy Research Network (ODPRN) and the OPDP set out to characterize the 10% of Ontario Drug Benefit (ODB) Program beneficiaries responsible for the highest expenditures.
Methods: We used a cross-sectional design to identify the 10% of ODB beneficiaries with the highest aggregate drug expenditures in each fiscal year from 2006/07 to 2010/11. Individuals were ranked based on total drug expenditure and the top 10% were defined as "high cost" beneficiaries.
Results: The proportion of total ODB expenditures attributed to high cost beneficiaries increased over time, from 44% ($1.29 billion) in 2006/07 to 52% ($1.68 billion) in 2010/11. Medication use among the high cost population was similar to that of all other ODB beneficiaries, with statins, antipsychotic agents, and cholinesterase inhibitors responsible for the highest costs in 2010/11. However, in the high cost group, expenditures were also driven by biological response modifying agents, ranibizumab, and opioids. The mix of medications with the highest costs in this group varied over the study period, reflecting the addition of immunosuppressive agents, insulins, and ranibizumab to the formulary.
Conclusions: Ten percent of ODB beneficiaries accounted for more than half of ODB expenditures in 2010/11. Further research is needed to understand the health care needs of this important and growing patient population.
Keywords: *Cost analysis, Ontario Drug Benefit, health resource use*

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Impact of maternal asthma, its severity and control, on the risk of abortions

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Background: Little is known about the impact of maternal asthma on the risk of spontaneous and induced abortion. We examined here whether or not women with asthma, and more specifically those with severe and uncontrolled asthma, are at higher risk of these outcomes.
Methods: A cohort of pregnancies from asthmatic (n=15,277) and non-asthmatic (n=34,687) women was reconstructed by linking three Quebec administrative databases between 1992 and 2002. We performed a case-control analysis of this cohort with 22,998 cases of abortions (7,814 spontaneous and 14,515 induced) and 26,966 deliveries which served as controls. Maternal asthma was defined by at least one asthma diagnosis and one dispensed prescription for an asthma medication in the two years prior to or during pregnancy. Asthma severity and control were assessed in the year prior to pregnancy with validated indexes. Logistic regression models were used for statistical analyses.
Results: The proportions of women with mild, moderate and severe asthma were 77.3%, 15.1% and 7.6%, respectively and 46.2% had uncontrolled asthma prior to pregnancy. The prevalence of spontaneous and induced abortions was 15.6% and 29.0%, respectively. Maternal asthma was associated with an increased risk of spontaneous abortion (OR: 1.40; 95%CI: 1.32-1.48) and a decreased risk of induced abortions (0.90; 0.86-0.94). No association was observed between asthma severity and abortion, while uncontrolled asthma augmented the risk of spontaneous abortion (1.22; 1.10-1.37).
Conclusions: Pregnant women with asthma, notably when uncontrolled, are at higher risk for spontaneous abortion. Our findings emphasize the importance of maintaining good asthma control prior and during pregnancy.
Keywords: *Asthma, pregnancy, spontaneous abortions, induced abortions, asthma severity and control*

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Impact of physician and technology factors on the adoption of personalized genomic diagnostics in breast cancer

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Background: The gene expression profiling assay, Oncotype DX® is used to predict the likelihood of breast cancer recurrence and the patients most likely to benefit from adjuvant chemotherapy. The objective was to determine the association between specific characteristics of Oncotype DX® and oncologists' intention to use Oncotype DX® to make treatment decisions for breast cancer patients.
Methods: An online survey of a nationally representative panel of oncologists treating breast cancer was conducted. A questionnaire was designed to study physicians' intentions to use Oncotype DX® and evaluate physicians' perceptions of specific characteristics of Oncotype DX® and how these might either facilitate or serve as a barrier to using Oncotype DX® for making treatment decisions for breast cancer

patients. Linear regression analysis was performed to establish the association between physicians' perceptions and intentions to use Oncotype DX®.
Results: A total of 119 completed surveys were received giving a response rate of 51.11%. Of the Oncotype DX® test characteristics evaluated, validity of the test' (p= 0.006) and 'use of Oncotype DX® by fellow Oncologists' (p=0.0068) were significantly associated with oncologists' use of Oncotype DX® Oncologists' intention to use Oncotype DX® increased consistently with their perceived usefulness of Oncotype DX® (β=0.222).Insurance status of the patients was also significantly associated with physicians' use of Oncotype DX® (p=0.008).
Conclusions: Several characteristics related to Oncotype DX® impact oncologists' intention to use Oncotype DX in the clinical setting to make treatment decisions for breast cancer patients. This study has implications for knowledge translation efforts related to novel personalized genomic medicine applications.
Keywords: *Knowledge translation, personalized medicine, breast cancer, gene expression profiling*

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Interventions that improve adherence to oral antidiabetic in adults with type 2 diabetes: a systematic review

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Background: Poor adherence to drug treatment is a concern, particularly in chronic conditions including diabetes. Few interventions to improve adherence have been proven effective and little is known on the characteristics of effective interventions.
Objectives: To evaluate the quality of studies on intervention aiming at improving adherence to oral antidiabetic drugs treatment (OADT) in adults with type 2 diabetes (T2DM) and to describe the characteristics of interventions that are most likely to succeed.
Methods: We carried out a systematic review using PubMed, Embase and the Cochrane Library. All databases were searched from their start date until October 2011. Studies were included if at least one component of the intervention aimed to improve adherence to OADT in adults with T2DM. Quality of studies (poor, medium or good) was evaluated using nine criteria recognized as essential in the report or planning of intervention studies. Characteristics of studies with at least medium overall quality and for which interventions had a positive effect on adherence were described.
Results: Among the eight studies included five had at least a medium overall quality score and two had a positive effect on adherence. Characteristics of effective interventions were: the use of socio-ecological theory; the use of behavioral determinants as empowerment, self-efficacy and barriers to medication; specific behavior change techniques. Interventions that were effective were delivered by health educators and mostly via phone calls.
Conclusion: The characteristics of identified effective interventions could inform in the planning of new interventions to improve adherence to OADT.
Keywords: *Intervention, medication adherence, type 2 diabetes*

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Intra-arterial thrombolysis versus standard treatment or intravenous thrombolysis in adults with acute ischemic stroke: a systematic review and meta-analysis

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Background: Recent evidence has suggested that intra-arterial thrombolysis (IAT) may provide benefit beyond intravenous thrombolysis (IVT) in ischemic stroke patients. Previous meta-analyses have only compared IAT to standard treatment [without thrombolysis]. The objective was to review the benefits and harms of IAT in ischemic stroke patients.
Methods: EMBASE, MEDLINE, the Cochrane registry and the stroke trials registry were queried from inception to 2011. Two reviewers independently screened titles and abstracts for randomized controlled trials of ischemic stroke comparing IAT to either IVT or standard treatment. Primary outcomes included good functional outcome, mortality and symptomatic intracranial hemorrhage. Results were stratified by comparison treatment.
Results: 543 citations were identified. Two trials (n=81) compared IAT to IVT while four trials (n=351) compared IAT to standard treatment. IAT increased good functional outcome by 47% when compared to standard treatment (RR=1.47; 95%CI=1.07-2.22; I2=0) and 74% when compared to IVT (RR=1.74; 95%CI=1.01-3.01; I2=0). IAT did not increase mortality compared to standard treatment (RR=0.82; 95%CI=0.56-1.21; I2=0) or IVT (RR=1.12;

95%CI=0.47-2.68; I2=0). However, symptomatic intracranial hemorrhage was almost four times higher with IAT when compared to standard treatment (RR=3.90; 95%CI=1.41-10.76; I2=0) while not significantly different compared to IVT (RR=1.13; 95%CI=0.32-3.99; I2=42%).
Conclusions: Compared to standard therapy or IVT, IAT increases good functional outcomes with no corresponding increase in mortality. However, IAT increases symptomatic intracranial hemorrhage compared to standard treatment while the risk remains comparable to IVT. Imprecise pooled estimates for good functional outcome prevent any overtly strong recommendation for the use of IAT.
Keywords: *Stroke, intra-arterial thrombolysis, systematic review*

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Multi-criteria decision analysis: how does Canada measure up?
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Background: Introduction of the Common Drug Review has resulted in a significant drop in the proportion of new drugs listed on provincial formularies. Recommendations and decisions around the value of innovative drugs are driven by stringent clinical evidence requirements, a narrow focus on cost-effectiveness, and review from the drug plan perspective only. Quebec's preference for a societal pharmacoeconomic perspective and analyses of net population health and cost impacts appears to result in improved access. Multi-criteria decision analysis (MCDA) has been proposed to further facilitate multi-stakeholder, transparent, and efficient decision-making. To understand the benefits of MCDA and its implementation barriers, a workshop was held to examine global experience with MCDA.
Methods: Panellists from the U.K., U.S., Sweden, Germany, Brazil, and Canada presented their views on MDCA in their countries. Audience members representing a cross-section of Canadian stakeholders then rated the importance of various criteria in decision-making and ranked barriers for identifying, weighting, and implementing criteria in the Canadian context.
Results: International experience and success with MCDA is variable. Although, inclusion of patient and lay person input into Canadian formulary review is commendable, the current framework does not elucidate how other important factors such as disease severity, ethical, social and political factors are considered. The complexity of MCDA remains a barrier in all countries.
Conclusions: Internationally, the will to implement MCDA into drug funding decisions exists but experience has been variable. Further work is required in Canada to formulate a process that can be applied across provinces and across disease areas.
Keywords: *Multi-criteria decision making, innovation, cost-effectiveness*

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No starting point bias with the bidding game in a willingness-to-pay analysis
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Background: Various instances of starting point bias in bidding games of willingness-to-pay (WTP) analyses have been reported in the literature. The present study aimed to determine if starting point bias was introduced in the bidding game of a WTP analysis.
Methods: In an online survey, members of the general public in Ontario, Canada, were presented descriptive and clinical information on two treatment delivery options (inhaler vs. injection) for a treatment of pulmonary arterial hypertension. Participants were then asked to select their preferred treatment delivery option and, if they chose the inhaler, to take part in a bidding game in order to ascertain their WTP in terms of additional monthly insurance premiums, having been randomly assigned one of three starting values (CAD$1, $2 or $5). The bidding game oscillated between a minimum of CAD$0.01 and a maximum of CAD$50.00, although participants could explicitly input a higher WTP, if desired. The potential differences in mean WTP associated with each starting value were evaluated by applying the Kruskall-Wallis non-parametric test.
Results: Study subjects selecting the inhaler (n=149) reported a mean WTP of CAD$43.86 in additional monthly insurance premium with a mean WTP of CAD$50.03, CAD$42.99 and CAD$39.23 attributable to a starting point of CAD$1, $2 or $5, respectively. No significant difference in WTP values was observed between the groups.
Conclusion: There appeared to be no starting point bias in the bidding game in the present study.
Keywords: *Willingness-to-pay, bidding game, bias*

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Perceptions of community pharmacists regarding their involvement in the management of osteoporosis and the risk of falls

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Funding Source: Reseau quebecois de recherche sur l'usage des medicaments (RQRUM) and Agence de la sante et des services sociaux de Laval

Background: A cross-sectional study was conducted to explore the perceptions of community pharmacists in urban and semi-urban areas regarding their ideal and actual levels of involvement in providing services related to the management of osteoporosis and the risk of falls and the barriers to such involvement.

Methods: Using a modified version of Dillman's tailored design method, a questionnaire including 28 multiple-choice or open-ended questions was mailed to a random sample of 1250 community pharmacists practicing in Montreal and surrounding areas. Results are reported using means with standard deviations for continuous variables and proportions for discrete variables.

Results: A total of 571 (45.7%) eligible community pharmacists completed and returned the questionnaire. Most pharmacists believed they should be very involved (43%) or involved (46%) in osteoporosis-related services, and very involved (34%) or involved (50%) in services related to the risk of falls. When asked about their everyday involvement in osteoporosis, pharmacists reported providing counseling when dispensing medications (77%), distributing written information (44%), and referring patients to external resources (21%). Regarding the risk of falls, the majority of respondents reported providing counseling when dispensing medications (56%) or no services (22%). Main barriers to the provision of these services in current practice were lack of: time (78%), clinical tools (65%), coordination with other healthcare professionals (54%), staff or resources (49%), and financial compensation (44%).

Conclusions: Although community pharmacists consider they should be involved in the management of osteoporosis and the risk of falls, many organizational barriers limit their actual involvement.

Keywords: *Community pharmacists, cross-sectional study, osteoporosis*

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Post-traumatic use and cost of analgesics and arthritic-related medications following lower-limb joint injuries in the population of the province of Quebec, Canada

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Background: Trends in post-traumatic use and cost of analgesics and arthritic-related medications are lacking. The aim of this study was to determine the yearly mean number and cost of analgesics and arthritic-related drug claims per individual following lower-limb joint injuries in the province of Quebec, Canada.

Methods: This was a population-based observational study. Quebec residents who had a fracture or dislocation of a lower-limb joint between 1998 and 2002 were identified from the Quebec Trauma Registry. The pharmaceutical services of the individuals covered by the Quebec public drug regimen (RAMQ) were reviewed to determine the yearly mean (SD) number and cost of analgesics and arthritic-related drug claims per individual during a five-year post-injury follow-up.

Results: There were 5106, 3645, 2445, 1601 and 879 individuals covered by the RAMQ with ≥1 analgesic or arthritic-related drug claim in the respective five years of follow-up. After a hip injury, the yearly mean (SD) number of analgesics and arthritic-related drug claims per individual increased from 16.94 (24.48) in the first year to 21.55 (29.41) in the fifth year. The yearly mean (SD) out-of-pocket and RAMQ costs per individual increased from $72.42 (82.83) and $288.76 (539.33) in the first year to $87.54 (96.36) and $400.59 (495.86) in the fifth year, respectively. The yearly mean number and costs of analgesics and arthritis-related drug claims per individual also increased after knee and ankle injuries.

Conclusions: The mean number and cost of analgesics and arthritis-related drug claims per individual increase within five years following lower-limb joint injuries.

Keywords: *Post-traumatic arthritis, drug utilization, governmental drug claims administrative database*

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Predictors of caffeine intake during pregnancy

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Background: Despite governmental recommendations to pregnant women on the reduction of caffeine intake, many recent studies report that a considerable proportion of them maintain this consumption during their pregnancy.
Objectives: To quantify the prevalence and identify the predictors of caffeine intake during pregnancy.
Methods: A questionnaire was mailed to 8505 women selected from the Quebec Pregnancy Registry. This Registry was created with the linkage of three administrative and hospital databases: Regie de l'assurance maladie du Quebec (RAMQ), Med-Echo, and l'Institut de la statistique du Quebec (ISQ). Eligible women were continuously insured by the RAMQ drug plan for at least 12 months before and during pregnancy, and gave birth to a live born infant between January 1998 and December 2003 in Quebec. Questionnaire data were linked to the Registry data and responders constituted the study population. Descriptive statistics and multivariate logistic regression models were performed.
Results: Among the 3345 women (39.4%) who answered the questionnaire, 2877 (87.3%) consumed caffeine before pregnancy and 2299 (71.8%) continued their consumption during pregnancy. Maternal age, place of birth (rural/urban), medication insurance status, maternal hypertension, hospitalisation and smoking before pregnancy were all increasing the likelihood of caffeine intake during pregnancy; higher education level and illicit drug use were decreasing the **likelihood of caffeine intake during gestation.**
Conclusions: Caffeine intake is common during pregnancy. Given that the risk of caffeine use during gestation remains controversial, predictors identified in this study will help physicians identify women that could potentially be at risk.
Keywords: *Caffeine pregnancy predictors*

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Preliminary results from the baseline questionnaire of the burden of bowel dysfunction in spinal cord injury study

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Funding Source: Ontario Neurotrauma Foundation

Background: Bowel dysfunction (BD) or difficulties evacuating/retaining stool are an expected complication experienced by the estimated 40,000 Canadians living with spinal cord injury (SCI).
Methods: This is a prospective, observational study with 80 adult participants to be recruited from three tertiary academic rehabilitation centres in Ontario, Canada. Participants complete nine questionnaires (baseline, three weekly and five monthly). Information related to demographics, BD (e.g., neurogenic bowel dysfunction score), health preference (e.g., Health Utilities Index Mark 3 (HUI-3)) and resource utilization (e.g., medications, supplies) attributed to BD is being collected.
Results: Preliminary results from one clinic (N=19) were evaluated. The majority (68.4%) were male and mean time post SCI was 18.1 +/- 10.4 (3 - 42) years. Seven participants were employed. Mean neurogenic BD score was 14.2 +/- 4.8 (7 - 24) out of 47 and mean HUI-3 score was 0.21 +/- 0.30 (-0.37 - 0.95) out of 1. The cohort was under the care of their primary physician for an average of 8.3 +/- 8.6 (0 - 33) years. Resource-wise 78.9% required supplies related to bowel care, and 26.3% received personal care and mean time was 95.6 +/- 51.1 (13 - 150) hours per month to assist with bowel care.
Conclusions: Preliminary results from 19 SCI individuals with BD indicate a variety of health resources being utilized. Once data collection has been completed, the average cost of bowel program implementation due to BD will be determined by multiplying the average number of resources by their unit cost.
Keywords: *Resource utilization, utilities, questionnaire*

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Programme ProFil - A training-and-communication network program in nephrology: An interim analysis

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Background: Chronic kidney disease (CKD) is highly prevalent. ProFiL, a training-and-communication network program, was created to support community pharmacists in the management of these patients. It includes an interactive web-based training program supported by a clinical guide as well as access to essential clinical data and to a consultation service offered by pharmacists with expertise in nephrology.
Objectives: The objectives of this interim analysis were to describe the prevalence of drug-related problems (DRPs) and the current knowledge and skills of community pharmacists about CKD.
Methods: In a cluster randomized controlled trial, patients were recruited in predialysis clinics. Their community pharmacies were randomized to the ProFiL or the Usual Care (UC) group. Patients' characteristics at baseline were documented and DRPs were assessed. Pharmacists' knowledge was documented at baseline using a self-administered questionnaire.
Results: 169 patients (ProFiL: 118; UC: 51) and 81 pharmacies (ProFiL: 53; UC: 28) participated. Patients were mostly men (60%) with a mean age of 66 year old (SD=13) suffering from severe CKD (59%). A mean of 3.5 and 3.6 DRPs per patient (SD: 2.1) were detected in the ProFiL and the UC, respectively. Most pharmacists were women (66%) with a mean of 10.8 years (SD=9.5) of experience. Their knowledge scores were similar in the two study groups (ProFiL: 68.9%; UC: 70.2%).
Conclusions: These results support the relevance of the ProFiL program for community pharmacists: the prevalence of DRPs in CKD patients is high and the current knowledge and skills of community pharmacists is not optimal.
Keywords: *Programme ProFil, chronic kidney disease, PAIR criteria*

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Systematic review of the literature on starting point bias in the bidding games of willingness-to-pay analyses

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Background: A systematic review of willingness-to-pay (WTP) analyses was undertaken to ascertain if any bias associated with the starting point (SP) of bidding games (BG) was reported in the literature.
Methods: OVID MEDLINE® (1996-2011) was systematically searched using the keywords [Bidding AND (Willingness to pay OR Willingness-to-pay OR WTP)] for WTP analyses applying more than one SP to a BG and discussing any associated bias. This process and the subsequent data extraction were undertaken independently by two reviewers; any discrepancy was resolved through consensus.
Results: The literature search yielded 51 articles, of which 12 met the inclusion criteria (primary evidence) and a further 5 reported on SP bias without presenting numerical data (secondary evidence). Primary evidence publications were based in Asia (k=4), North America (k=3), Africa (k=3) and Europe (k=2), and targeted the general public (k=7), patients (k=4) or both (k=1). Most primary (7/12) and secondary (4/5) evidence publications reported a SP bias on the results of the BG. The associations between various analytic factors and the occurrence of starting point bias were examined and will be reported.
Conclusions: Evidence of SP bias has been reported in the literature, without however a clear definition of the conditions under which such bias appears.
Keywords: *Willingness-to-pay, bidding game, bias*

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Systematic review of the case-crossover design in pharmacoepidemiology

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Background: The case-crossover study is an emerging design in pharmacoepidemiology that is advantageous to control for time-invariant confounding and when the risk-/benefit-window is short.
Methods: We conducted a systematic search of EMBASE and MEDLINE to identify all English-language articles that employed a non-experimental case-crossover study design. Review papers, methodological contributions and empirical pharmacoepidemiologic applications were eligible and pulled for detailed review. The number of publications was tabulated by year and the methods employed in empirical pharmacoepidemiologic applications were summarized.
Results: Of 131 eligible papers, we identified 39 review papers, 34 methodological contributions, and 58 pharmacoepidemiologic applications published between 1991 and 2012. The first pharmacoepidemiologic

application was published in 1995. A gradual increase has since been observed with 1 pharmacoepidemiologic application published in 2000 to a high of 15 published in 2011. The case-crossover design was mainly applied to studies examining drug safety (92%), followed by studies examining predictors of treatment re-initiation (5%), and drug effectiveness (3%). NSAIDs (17%), cardiovascular (10%), anti-depressants (10%), and antibiotics/anti-infectives (7%) were the most common drug exposures examined; and hospital admission (21%), cardiovascular disease or stroke (19%) and infectious disease (9%) were the most commonly studied outcomes. The most commonly applied hazard windows were 30-day (19%), and 1-day (16%) in length.

Conclusions: Use of the case-crossover design in pharmacoepidemiology has increased in the last decade. As the application of the case-crossover design continues to increase, it is important to develop standards of practice.

Keywords: *Case-crossover, pharmacoepidemiology, systematic review*

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The burden of type 2 diabetes on work productivity: a systematic review

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Funding Source: This study was funded by the Chair on Adherence to Treatments. This Chair is supported by a non-restricted grant from AstraZeneca, Merck Canada, Sanofi-aventis Canada, Pfizer, and from the "Prends soin de toi program" (a Quebec provincial program for the improvement of public health, focused on mental health disorders).

Background: Type 2 diabetes is a common disease which may impact employees, employers, payers and society in terms of lost productivity at work.

Objective: To describe the risk and magnitude of work productivity losses among individuals in the labour force with type 2 diabetes as compared to those without diabetes.

Methods: A systematic review was conducted through a literature search of published studies using Medline, Embase, Psych-Info, Proquest and the Occupational Health and Safety reference collection. Databases were searched from their start date until June 2011. No language restriction was applied. Studies were included if: 1) the effect of type 2 diabetes on absenteeism, presenteeism, productivity loss, unemployment/employment, disability or early retirement was measured; 2) a cross-sectional, cohort or case-control design was used. Two authors independently selected studies, extracted data and assessed quality. Since there was substantial heterogeneity among studies, our synthesis is reported in the form of a descriptive analysis.

Results: Twenty-six studies were included. Type 2 diabetes was significantly associated with an increase in productivity loss or retirement in all of the 9 studies focusing on these outcomes. A significant trend toward increased absenteeism, employment and disability was observed in 16 of the studies. No consistent data was available for presenteeism. The quality of studies was variable.

Conclusions: Type 2 diabetes seems to have a considerable impact on lost productivity at work. There is a need for interventions targeting workers as the burden of type 2 diabetes is likely to increase in the coming years.

Keywords: *Type 2 diabetes, work productivity, systematic review*

ENCORE PRESENTATION

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The effect of bupropion on symptoms of depression among patients attempting to quit smoking post-myocardial infarction: The ZESCA Trial

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The effect of SABA and LABA on fetal development and prematurity among asthmatic women: an updated

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Funding Source: This study was funded through a research grant received from the Canadian Institutes of Health Research (CIHR)

Background: Short and long acting beta-2-agonists (SABA and LABA) have a crucial role in asthma management during pregnancy and current guidelines suggest their safety. However, their fetal safety data is scarce.
Objective: To perform a systematic review of the existing literature examining SABA and LABA effect on fetal development and prematurity.
Methods: Studies investigating SABA and LABA use during pregnancy and fetal development, represented by congenital malformations and mean birth weight, and prematurity, represented by gestational age and preterm delivery were searched in PubMed, Ovid MEDLINE, EMBASE, Cochrane Library, Web of Science, and CINAHL before January 1, 2012. Quality assessment and post-hoc power calculations were performed for each study.
Results: Twenty-four original studies were retrieved. Regarding fetal development, four studies reported a significant increased risk of congenital malformations with SABA use, and one study reported a significant decreased risk with high doses of SABA. One study reported a significant increased risk of malformations with LABA use and three studies reported a significant increased risk of malformations with SABA and LABA combined. For mean birth weight, one study reported a decrease in birth weight centiles among LABA users. On the other hand, neither SABA nor LABA use showed an effect on the prematurity of infants.
Conclusion: SABA use, LABA use and their combined use during pregnancy presented significant effects on fetal development, but not on infants' prematurity. Nonetheless, non-significant results should be interpreted with caution due to the low statistical power and modest quality of several studies.
Keywords: *Beta-2-agonists, pregnancy, systematic review*

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The impact of unmeasured confounders in cardiovascular studies performed in administrative databases

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Background: Administrative databases are increasingly being used in pharmacoepidemiology. However, given that important confounders are often missing in these databases such as smoking, body mass index, and other clinical variables, and that they are seldom truly population-based, studies using them are often criticized. Hence, the aim of our study was to estimate the impact of unmeasured confounders in the association between antihypertensive (AH) and statin therapy and the risk of cardiac events, stratified on patient gender.
Method: Data were obtained from two administrative databases from Quebec (RAMQ and Med-Echo) and a mailed auto-administered questionnaire. Estimates of bias for six potential confounders (obesity, physical activities, smoking, alcohol, income and cardiovascular family history) were calculated using the method proposed by Schneeweiss for three different study populations (workers, welfare recipients, and elderly), stratified by gender. Estimates of bias were calculated for each confounder individually as well as for all confounders combined.
Results: 6,453 subjects returned their questionnaire, and were included in this study. We found that the bias for the non-adjustment of these six potential confounders was different for males and females in each study population. The combined bias was -4.2% and -0.7% for male and female workers, respectively, meaning that non-adjustment would lead to an underestimation of the association between AH/statin use and the risk of cardiac events. Similar gender differences in bias estimates were observed in the other study populations.
Conclusion: We have shown that unmeasured confounders can have a significant impact on risk estimates. The impact is dependent on patient gender.
Keywords: *Potential confounders, bias, administrative databases, external data, Schneeweiss method*

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The risk of venous thromboembolism of drospirenone-containing combined oral contraceptives: a systematic review and meta-analysis

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Background: Previous studies have reported conflicting results regarding the effect of drospirenone-containing combined oral contraceptives (COCs) on the risk of venous thromboembolism (VTE). We therefore conducted a meta-analysis to compare the risk of VTE in individuals taking drospirenone-containing COCs to that in individuals taking levonorgestrel-containing COCs.
Methods: We systematically searched the literature from inception to July 2011 for observational and experimental studies comparing the risk of VTE between drospirenone-containing COCs and levonorgestrel-containing COCs. Data were aggregated using a random-effects meta-analysis model.
Results: A total of 4 studies (1 cohort study, 1 case-control study, and 2 nested case-control studies) involving 44,384 women of reproductive age, were included. In individual studies, the relative effect of drospirenone-containing COCs on the risk of VTE ranged from 1.0 (95% confidence interval [CI] = 0.5, 1.8) to 3.3 (95% CI = 1.4, 7.6). When data were pooled across studies, drospirenone-containing COCs appear to increase the rate of VTE compared with levonorgestrel-containing COCs (rate ratio = 1.64, 95% CI = 0.93, 2.91).
Conclusions: Although not conclusive, our results suggest that drospirenone-containing COCs may be associated with a higher risk for VTE than levonorgestrel-containing COCs. Our study highlights the need for additional studies examining the safety profile of drospirenone-containing COCs.
Keywords: *Combined oral contraceptives, drospirenone, venous thromboembolism*

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The role of community pharmacists in health promotion and prevention: a cross-sectional study

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Background: A cross-sectional study was conducted to explore the perceptions of community pharmacists in urban and semi-urban areas regarding their ideal and actual levels of involvement in providing health-promotion and prevention services and the barriers to such involvement.
Methods: Using a modified version of Dillman's tailored design method, a questionnaire including 28 multiple-choice or open-ended questions was mailed to a random sample of 1250 pharmacists practicing in Montreal and surrounding areas. Results are reported using means with standard deviations for continuous variables and proportions for discrete variables.
Results: A total of 571 (45.7%) eligible community pharmacists completed and returned the questionnaire. Most believed they should be very involved in health promotion and prevention, particularly in smoking cessation (84%); screening for hypertension (82%), dyslipidemia (57%) and diabetes (76%); and sexual health (62% to 89%). However, fewer respondents reported actually being very involved in providing such services (6%, 45%, 7%, 35% and 19%, respectively). Main barriers to the provision of these services in current practice were lack of: time (86%), coordination with other health care professionals (61%), staff or resources (57%), financial compensation (51%), and clinical tools (46%).
Conclusions: Although community pharmacists think they should play a significant role in health promotion and prevention, they recognize a wide gap between their ideal and actual levels of involvement. The efficient integration of primary care pharmacists and pharmacies into public health cannot be envisioned without addressing important organizational barriers.
Keywords: *Community pharmacists, cross-sectional study, health promotion and prevention*

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Thromboprophylaxis patterns in patients undergoing elective total knee and hip replacement surgery in the province of Quebec

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Funding Source: This project was funded by Bristol-Myers Squibb Canada and Pfizer Canada

Background: Venous thromboembolism (VTE) is a well-known complication of total hip and knee replacement (THR/TKR). Recently, novel oral anticoagulants (NOACs) were evaluated against enoxaparin, a low molecular weight heparin (LMWH) for the prevention of VTE in patients undergoing elective THR/TKR. While Health Canada recommends a 30mg BID dose for enoxaparin, the 40mg QD dose is recommended in other countries. This analysis aims to characterize thromboprophylaxis utilization, specifically enoxaparin, in patients with elective THR/TKR at hospital discharge in Quebec.
Methods: This study was performed using data from the Quebec provincial medical and drug plans (Regie de l'assurance maladie du Quebec) for adult patients undergoing THR/TKR between January 1, 2008 and March 31, 2009. Due to data availability, only public drug plan patients discharged home from hospital were included. Patients in nursing homes or rehabilitation centers were excluded.
Results: Of the 4,311 patients extracted from the database, 4,171 were eligible for inclusion in the study. Of those, 2,368 (56.8%) and 1,803 (43.2%) had TKR and THR, respectively. Pharmacological thromboprophylaxis was dispensed to 73.9% (n=3,086) of the cohort at discharge, with the majority (81%; n=2,505) receiving a LMWH. Of those, 53.7% (n=1,346) received enoxaparin. Amongst enoxaparin patients on either 30mg or 40mg, 41.9% were dispensed the 40mg strength.
Conclusions: This study shows that LMWHs are the most dispensed thromboprophylaxis for TKR/THR patients in Quebec, with enoxaparin the most used LMWH. Approximately 40% of enoxaparin patients were dispensed the 40mg strength, underlining the relevance of clinical trials comparing NOACs with both regimens of enoxaparin.
Keywords: *Thromboprophylaxis, joint replacement surgery, enoxaparin*

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TRANSIT: a primary care interprofessional intervention program to improve the management of cardiovascular risk factors in patients with multiple chronic conditions

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Background: In primary care (PC), the management of cardiovascular risk factors is often suboptimal. The Chronic Care Model (CCM) is a guide for the development of effective chronic disease management. However, such interventions cannot be easily defined and implemented. In participatory research, PC community identified collaborative practices and self-management support as priorities for action to improve cardiovascular prevention.
Objective: With the PC community, translate those priorities in an interprofessional intervention program to manage cardiovascular risk factors in multimorbid patients.
Methods: Members of the PC community, including clinicians, health managers, researchers, administrative support staff, and patients and family members took part in 3 large group meetings and 2-3 sub-group meetings to develop the intervention program. Other members of the community and professional corporations contributed to its validation.
Results: Preventive care is provided by a team of PC clinicians. Nurse assumes a pivotal role by coordinating interprofessional care. She performs motivational interview, evaluates family support, and refers patient when appropriate to other PC clinicians (nutritionist, kinesiologist, psychologist, tobacco cessation expert, and pharmacist). Advanced nursing and pharmaceutical care is supported by collective prescriptions. Patients are actively involved in the selection of their treatment plan, which is supported by a health booklet and an electronic directory of available regional health resources.
Conclusions: The TRANSIT program is based on the CCM and was developed by and for the PC community, which ensures optimal relevance and applicability. TRANSIT will be implemented in a pragmatic trial, where 2 implementation strategies will be tested: facilitation and passive diffusion.
Keywords: *Primary care, community-based participatory research interprofessional collaboration prevention of cardiovascular disease*

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Trends in dispensations of high dose folic acid and birth prevalence of major congenital malformations

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Background: In 2007, the Society of Obstetricians and Gynaecologists of Canada (SOGC) introduced new guidelines on the use of folic acid aimed at further reducing the prevalence of neural tube defects (NTDs).The new guidelines recommended increased folic acid intake in specific groups of the population. In Quebec, this dosage is only available with a prescription and reimbursed by the public drug plan. Our objective was to assess the impact of these new guidelines on the number of women having high dose periconceptional folic acid intake.
Methods: We used the Quebec Pregnancy Registry to analyze trends in high dose folic acid (5 mg daily) dispensations before or during pregnancy between January 1998 and December 2008. Annual trends were analyzed using the Cochran-Armitage test.
Results: We identified 157,796 pregnancies ending in a delivery. According to our folic acid exposure definition, the annual percentage of pregnancies exposed to high dose folic acid increased from 1998 (0.17%) to 2008 (0.80%) (p for trends < 0.0001).
Conclusions: During this 10-year period, there was an increase in the use of high dose folic acid during pregnancy; we can suppose that this is also the case for low dose folic acid. The next step will be to assess whether this augmentation is accompanied with a decrease in birth prevalence of NTDs and other major congenital malformations.
Keywords: *Folic acid, major congenital malformations, pregnancy*

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Using anonymized longitudinal patient data to monitor the impact of formulary differences on patient treatment when transitioning from private to public coverage in Canada

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Funding Source: IMS Brogan provided time and access to the data for analysis.

Background: The power of large scale anonymized patient level information can efficiently be used to better understand the Disease Treatment of Canadians across cash, private and public reimbursement channels. Longitudinal prescription data (Lifelink LRx) were examined to obtain a better understanding of the impact of formulary differences across these channels.
Methods: Public formularies can take years to list a medication, and listing is not guaranteed (approximately 50% of products get a positive listing recommendation from CDR). As a result, Canadians exiting the workforce on a stable course of therapy may be faced with reimbursement challenges when transitioning from private to public reimbursement. A longitudinal analysis of three patient cohorts based on different reimbursement profiles relative to formulary listing date were examined, to assess the impact of formulary on patient treatment.
Results: This analysis focused on OAD patients in Ontario who were being treated with Sitagliptin (Januvia), prior to formulary listing through non-public reimbursement. Patients with non-public coverage past the listing date were minimally impacted. Patients with both non-public and public coverage were also minimally impacted, however reimbursement flipped from non-public to public after listing. Over 75% of patients with only public coverage prior to listing dropped their stable treatment of Sitagliptin. After listing, some patients returned, however 65% of patients remained off Sitagliptin.
Conclusions: Although the focus of this work has been on one particular product-province combination, the power of Lifelink LRx can be leveraged by governments, pharmaceutical manufacturers, medical researchers, and other healthcare professionals, against almost any combination of products and provinces.
Keywords: *Reimbursement, patient treatment, lifelink*

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Validation of congenital malformation diagnostic codes recorded in Quebec administrative databases

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Background: Diagnoses recorded in administrative databases are primarily coded for billing purposes. We assessed the validity of the diagnostic codes of congenital malformations (CM) recorded in the Quebec databases among babies from mothers with and without asthma.
Methods: Using a large cohort of pregnancies from asthmatic and non-asthmatic women and their babies reconstructed from the linkage of three Quebec databases (1990-2002), we selected babies with and without CM. The diagnosis of CM derived from the RAMQ and MED-ECHO databases was compared to the diagnosis written in the baby's medical chart ("gold standard"). We estimated the predictive positive value (PPV) and the predictive negative value (PNV) for any CM identified from the databases. We also estimated the PPV for major CM and for several groups of CM.

Results: Selected babies from asthmatic women included 496 with at least one CM and 256 without CM recorded in the databases. The corresponding figures for babies of non-asthmatic women were 404 and 138, respectively. The PPV of having any or a major CM were 82.7% (95%CI: 80.0-85.4) and 79.2% (76.3-82.1), respectively, in the asthma group, while they were 82.2% (79.0-85.4) and 78.4% (74.9-81.8), respectively, in the non-asthma group. In both groups, PPVs >80% were found for several specific CM including cardiac, clefts, climbs, digestive, urinary and genital malformations. The PNV for any CM was 91.0% (89.0-93.1) in the asthma group and 94.2% (92.2-96.2) in the non-asthma group.
Conclusions: Quebec databases are a valid tool for epidemiological research on CM, with no differences observed between babies from asthmatic and non-asthmatic mothers.
Keywords: *Administrative databases, diagnostic codes, validity, congenital malformations*

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Vascular protection with ACE inhibitors or angiotensin II receptor antagonists following type 2 diabetes treatment initiation in elderly

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Background: Canadian practice guidelines recommend that ACE inhibitors (ACEIs) or angiotensin II receptor antagonists (ARBs) be used for vascular protection in people with diabetes at high risk of cardiovascular event including diabetics aged ≥65.
Objectives: To estimate the proportion of elderly who initiated either an ACEI or an ARB (ACEI/ARB) in the year following the beginning of an oral antidiabetes drug (OAD) treatment and to identify factors associated with this initiation.
Methods: Using the Quebec Health Insurance Board databases, we conducted a population-based cohort study of individuals aged ≥65 who were newly dispensed an OAD between 2000-01-01 and 2008-12-31 and had no claim for an ACEI/ARB in the preceding year. Factors associated with ACEI/ARB initiation were identified using multivariate logistic regression.
Results: Among the 43,700 study individuals, 13,621 (31.2%) initiated an ACEI/ARB in the year following OAD initiation. Individuals were more likely to initiate an ACEI/ARB if they initially received both metformin and a secretagogue, lived in a rural region, initiated their OAD between 2001 and 2006, were hospitalized or made >22 medical visits in the year preceding OAD initiation. Individuals aged ≥75, those who were prescribed an OAD by a general practitioner, initially received a secretagogue or received ≥4 different medications in the year preceding OAD initiation, were less likely to initiate an ACEI/ARB.
Conclusions: In the elderly not already taking ACEI/ARB, a low proportion of those undertaking an OAD treatment are initiated in the following year to the recommended cardio-protection of ACEI/ARB. Interventions are needed to close this gap.
Keywords: *Type 2 diabetes, vascular protection, elderly*

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When the risk of confounding by indication is high, are administrative data adequate to achieve scientific excellence in pharmacoepidemiology?

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Funding Source: None

Background: To perform an evaluation of aspects of the methodology of observational population-based research studies in which the risk of confounding by indication is high, using studies of the risk of acute myocardial infarction (AMI) associated with rosiglitazone.
Methods: The PubMed literature database was searched for articles published between January 2006 and December 2010 on observational cohort or case-control studies evaluating the risk of AMI in rosiglitazone recipients. The identified publications were reviewed against criteria from the Checklist for Retrospective Database Studies, developed by the International Society for Pharmacoeconomics and Outcomes Research, assessing aspects of the data source, research design, study population, statistical method and discussion of results.
Results: Nineteen rosiglitazone studies satisfied the inclusion criteria of the systematic review (13 retrospective cohorts; six nested case-control studies). The rationale for the data source and research design was absent or unclear in 84% and 95% of the studies, respectively. Three-quarters of the studies used administrative data exclusively, which resulted in important clinical variables being unavailable for assessing and adjusting for confounding. Only a third reported a formulary or reimbursement restriction, although some constraint on rosiglitazone use was likely to have been in place in all study settings. In two-thirds

of the treatment comparisons, what was being tested lacked specificity and clarity.

Conclusions: Important deficiencies existed in the methods used in the studies in this evaluation. In observational pharmacoepidemiology studies examining drug effects where the risk of confounding by indication is high, improvements in the methodological standard and reporting transparency are warranted.

Keywords: *Pharmacoepidemiology research, administrative data*

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