DOI: 10.22374/1710-6222.26.3.x

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

Driving Health Innovation: Harnessing the Power and Value of Real-World Evidence

ABSTRACTS

October 21st – 22nd, 2019
MaRS Discovery District
101 College Street
Toronto, Ontario

Abstracts are published on-line in
The Journal of Population Therapeutics and Clinical Pharmacology
www.jptcp.com

J Popul Ther Clin Pharmacol Vol 26(3):e14-e34; October 18, 2019.

ORAL PRESENTATIONS

1. The economic burden of CLL in Canada associated with the adoption of oral targeted therapy

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Background: Oral targeted therapy (OTT) for chronic lymphocytic leukemia (CLL) represents a major economic burden on the healthcare system. The objective of this study was to estimate future direct costs, as well as the prevalence, of CLL in the era of OTT in Canada.
Methods: The economic burden of OTT compared to chemoimmunotherapy (CIT) for treating patients with CLL was assessed from 2011 to 2025. For the OTT scenario, CIT was considered the standard of care before 2015, while OTT was considered for CLL patients with either unmutated immunoglobulin heavy-chain variable (IGHV) or del(17p)/TP53 mutations starting in 2015 and, from 2020 onwards, for all first-line treatments except for patients with mutated IGHV. A Markov model was developed including four health states: watchful-waiting, first-line treatment, relapse and death. Costs of therapy, follow-up/monitoring and adverse event were included. Key clinical parameters were extracted from pivotal clinical trials.
Results: As incidence rates and rate of survival are increasing, the prevalence of CLL in Canada is projected to increase from 8,301 in 2011 to 14,654 by 2025 (177% increase). Correspondingly, the total annual costs of CLL management will increase from $60.8 million to $957.5 million from 2011 to 2025, respectively (15.7-fold increase).
Conclusions: While OTT enhances survival for CLL patients, it is nonetheless associated with an important economic burden due to the projected vast increase in costs from 2011 to 2025. Changes in clinical strategies, such as implementation of a fixed OTT treatment duration or discontinuation and retreatment based on depth of response, would help alleviate financial burden.

2. Impact of patient-target financial incentives on healthcare costs: A systematic review of randomized controlled trials

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Objective: The objective of this study was to provide a comprehensive assessment of the impact of financial incentives of healthcare costs through a systematic review of health policy trials.
Methods: We searched electronic databases, clinical trial registries, and websites of health economic organisations to identify randomized controlled trials (RCTs) in which the intervention was a patient-targeted financial incentive and healthcare costs were included as an outcome. Two reviewers independently reviewed titles, abstracts and full texts to assess study eligibility using a piloted form. Due to heterogeneity between studies, results were synthesized qualitatively.
Results: 15,845 records were retrieved, of which 25 articles fulfilled the inclusion criteria, describing 15 RCTs. Ten RCTs were conducted in the United States and one each in Ghana, Nicaragua, India, Burkina Faso, and Mexico. The interventions comprised increased health insurance coverage and voucher or cash-back programs. Of the 17 articles

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that measured costs from the perspective of healthcare payers, 10 (58.8%) found no difference and 4 (23.5%) an increase in total healthcare costs. When evaluating specific cost components (e.g. ambulatory or preventative care), 9 articles (52.9%) found an increase in costs associated with the intervention. Of the 10 articles that measured the costs to patients, 6 (60.0%) found a significant decrease and 4 (40.0%) no difference in out-of-pocket costs (note: two articles included both perspectives).

Conclusion: Patient-targeted financial incentives decreased or had no impact on the cost to patients. This type of policy intervention might increase specific resource use but not the total costs to healthcare payers.

3. HIV treatment response among female sex workers participating in a treatment as prevention demonstration project in Cotonou, Benin

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Objectives: Female sex workers (FSWs) play a key role in HIV transmission in West Africa, while they have limited access to antiretroviral therapy (ART). In line with UNAIDS recommendations extending ART to all HIV-infected individuals, we conducted this demonstration project on immediate treatment as prevention (TasP) among FSWs in Cotonou, Benin. We report data on treatment response and its relation to adherence, as well as on ART-resistant genotypes.

Methods: Complete follow-up varied between 12 and 24 months. At each three-monthly visit, a questionnaire was administered, clinical examinations were carried out and blood samples collected. Adherence to treatment was estimated by self-report. Viral RNA was genotyped at baseline and final visits for drug resistance. Generalized estimating equations for repeated measures with a log-binomial link were used to analyze time trends and the association between adherence and virological response to treatment.

Results: One-hundred-seven HIV-positive and ART-naive FSWs were enrolled; 59.8% remained in the cohort till study completion and 62.6% had a final visit. Viral load <1000 (<40) was attained in 73.1% (64.6%) of participants at month-6, 84.8% (71.2%) at month-12, and 80.9% (65.1%) at the final visit. The proportion of women with suppressed (undetectable) viral load increased with increasing self-reported adherence (p = 0.06 (0.003), tests for trend). The proportion of participants with CD4 ≤500 also decreased drastically throughout follow-up (p<0001). Twelve participants exhibited ART-resistant genotypes at baseline, but only two at their final visit.

Conclusion: Our findings indicate that TasP is widely accepted among FSWs in Cotonou and could be implemented with relative success. However, due to mobility in this population, follow-up was sub-optimal, suggesting that large geographical coverage of FSW-friendly clinics is needed for sustained treatment implementation. We also fell short of the UNAIDS objective of 90% viral suppression among treated patients, underlining the need for better adherence support programs.

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4. Systemic Sclerosis (SSc) with Interstitial Lung Disease (SSc-ILD) in Canada's largest province: An estimate of the prevalence and survival of SSc and SSc-ILD in Ontario.

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Background: To date, no published study has generated Canadian population-based estimates of prevalence and survival of SSc-ILD. The objectives of this study included estimating the prevalence and mortality of SSc and SSc-ILD in Ontario, Canada using administrative data.
Methods: Adult patients diagnosed with SSc and SSc-ILD between April 1, 2008 and March 31, 2018 were abstracted from the National Ambulatory Care Reporting System and Discharge Abstract Database, using ICD 10 CA codes. Systemic sclerosis was defined using M34 codes (M34.0, M34.1, M34.2, M34.8, and M34.9) identified first and SSc-ILD patients were identified if an additional one of J84.1, J84.8, J84.9 or J99.1 was available after the SSc diagnosis. Prevalence estimates for both the SSc and SSc-ILD populations were generated for all eligible adults in Ontario (~10.5 million). Descriptive statistics and Kaplan-Meier curves were generated.
Results: 3,111 unique SSc patients were identified of which, 559 were SSc-ILD patients. Average annual prevalence of SSc and SSc-ILD over the study period was 13.73 per 100,000 and 2.36 per 100,000 persons, respectively. The mortality rates at one, five and ten years after diagnosis for the SSc group was 14.56%, 30.25% and 36.97%, respectively. The SSc-ILD group mortality rates at one, five and ten years were higher, at 22.54%, 51.34% and 63.69%, respectively.
Conclusions: This study provides the first population based prevalence and mortality estimates of SSc-ILD patients in Canada. Results confirm that the prevalence of SSc-ILD may fall within a potential Canadian threshold for drugs for "other" rare disease. SSc-ILD may have a higher mortality rate than SSc.

POSTER PRESENTATIONS

5. Baseline bone density testing in men starting androgen deprivation therapy for prostate cancer

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Background: Androgen deprivation therapy (ADT) is a cornerstone of advanced prostate cancer (PCa) treatment. However, it is associated with loss of bone mineral density (BMD) which increases fracture risk. Guidelines recommend BMD testing when initiating ADT to properly assess baseline fracture risk. The objective was to examine the proportion of BMD testing in men initiating ADT in Quebec.
Methods: The cohort extracted patients treated by long-term ADT from 2001-2015 from Quebec public healthcare administrative databases. The primary outcome was the receipt of baseline BMD testing (defined as a BMD test 6 months prior to and up to 12 months after ADT initiation. Multivariable generalized linear mixed regression with a logit link was performed to identify variables associated with baseline BMD testing.
Results: We identified 6,410 patients, of which 12.6% underwent baseline BMD testing. Rates of baseline BMD testing varied from 7.7% in 2001-2003 to 12.3% in 2013-2012. Following multivariable analyses, later years during the study period remained associated with higher odds of baseline BMD testing compared to the earlier years (2001-2003) (ORs from 1.43-1.88; all p<0.010). Conversely, older age (OR 0.73; 95% CI 0.57-0.94; p=0.001), greater comorbidity (OR 0.51; 95%CI 0.34-0.75; p=0.001),

and rural residence (OR 0.60; 95%CI 0.48-0.75; p<0.001) were associated with lower odds.
Conclusion: Rates of baseline BMD testing in men initiating ADT are low, although it increased over the study period. Potential gaps were identified in older, more comorbid patients, and rural areas. Overall, additional efforts emphasizing the importance of BMD testing in PCa guidelines are needed.

6. Economic impact of introducing a new dosing regimen for nivolumab in non-small cell lung cancer in Ontario

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Background: The funded dose by Ontario New Drug Funding Program (NDFP) for nivolumab was initially 3 mg/kg every 2 weeks (Q2W), up to a maximum of 240 mg as an intravenous infusion over 60 minutes for patients with metastatic pre-treated non-small cell lung cancer (NSCLC). Recently the NFDP decided to fund a new regimen of 6 mg/kg IV, up to a maximum dose of 480 mg, every 4 weeks as an intravenous infusion of 30 minutes (Q4W).
Objective: To assess the impact on drug budget, hospital chair time and patients' out-of-pocket costs of the new dosing regimen. Methods: The cost difference between the Q2W and the Q4W was calculated in terms of drug acquisition, hospital chair time, patients out-of-pocket for travelling and parking. All costs in 2018 Canadian dollar. The drug acquisition cost was based on the drug list price and the patient weight sourced from a company sponsored access program (Hope).
Results: The average weight reported for 467 patients from the Hope program was 70.7 kg. The monthly average drug costs per patient were $8,987, and $8,530 respectively for the Q2W weight based dosing, and the Q4W weight based with a maximum of 480 mg. The monthly cost per patient associated with hospital chair time and patients out of pocket were reduced respectively by $101 and $66 when shifting from Q2W to Q4W.
Conclusion: The reimbursement of Q4W by the Ontario NDFP has the potential to provide important savings to the Ontario Healthcare system and to the patients.

7. How personalized are the results of high-profile randomized trials of pharmacotherapy? A systematic review

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Background: Current standards of medical care recommend shared decision-making between providers and patients for choosing treatment options. Since patients require information on their own risk of benefit versus harm of taking a therapy compared to not taking the therapy, personalization of evidence has become an important endeavour. Randomized controlled trials (RCTs) are considered the highest level of evidence for comparison studies. Our objective was to review the degree of personalization in the reporting of recent high-profile RCTs involving pharmacological interventions.
Methods: We performed a systematic review of RCTs published between 2012 and 2017 with at least one intervention evaluating drug therapy and meeting the high-profile threshold in a premier high-quality literature abstraction service. Our primary outcome was the proportion of trials reporting subgroup analyses of a combined benefit-harm outcome. Secondary outcomes included the proportion

of trials reporting subgroup analyses or clinical prediction guides for benefits or harms. We assessed the quality of the subgroup analyses.
Results: Of 296 eligible RCTs, 9 (3%) studies reported a combined benefit-harm endpoint. Subgroup analyses were carried out in 3 (1%) studies reporting a combined benefit-harm endpoint, in 168 (56.8%) studies reporting a benefit outcome, and in 18 (6.1%) studies reporting a harm outcome. The overall quality of the subgroup analyses was poor. Only one study reported a clinical prediction guide.
Conclusions: Despite considerable interest and rationale, RCTs rarely include rigorous attempts to personalize drug therapies. Lack of widely accepted, high quality methods seems to be the major barrier.

8. Assessing the role of real world evidence in oncology health technology assessment submissions based on single-arm trials in Canada

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Background: Health technology assessment (HTA) agencies often rely on evidence from randomized controlled trials (RCT) to assess efficacy and incremental benefits to patients. However, increasingly, single arm trial (SAT) evidence is being utilized. The objective of this study was to investigate the role of real-world evidence (RWE) in supporting SAT data, and the impact on oncology HTA recommendations in Canada.
Methods: Publically available reports from Canadian Agency for Drugs and Technologies (CADTH) pan-Canadian Oncology Drug Review were reviewed between June 2014 and June 2019. The product, indication, trial data sources for the economic evaluation, recommendation and reasons for the recommendation were extracted by a single reviewer; each report was examined to identify which were based on SAT supplemented with RWE.
Results: Of 141 submissions reviewed, 108 had submission details and recommendations available. From these, 19 (17.6%) of the submissions were based on evidence from SAT. The majority of the indications were either a type of lymphoma (N=5) or chronic/acute leukemia (n=5). Of the 19 SAT submissions, 10 included RWE with the following recommendations: do not reimburse (n=5), and reimburse with clinical criteria or conditions (n=5). All but two submissions included RWE for use as historical control and/or matched case analysis. Of those with a positive recommendation (N=5), the majority were for aggressive rare cancers and a high unmet clinical need.
Conclusions: These findings support the notion that RWE is gaining traction in providing relevant data valuable for successful SAT submissions to Canadian HTAs

9. Time to Discontinuation of Tofacitinib in Rheumatoid Arthritis Patients with and without Methotrexate: Data From A Rheumatoid Arthritis Cohort

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Background: Tofacitinib (TOFA) is an oral, small molecule drug which can be used as an alternative to biologic disease modifying antirheumatic drugs (bDMARDs) for rheumatoid arthritis (RA) treatment and is prescribed alone or with methotrexate (MTX). We aimed to evaluate the discontinuation rate of this drug, with and without concurrent MTX, and with and without prior biologic use, in patients with RA in the Ontario Best Practices Research Initiative (OBRI).
Methods: RA patients enrolled in the OBRI initiating their TOFA within 30 days prior to or any time after enrolment between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2017 were

included. Patients were excluded if they had 2 visits and 6 months follow-up. Time to discontinuation due to (1) any reason, (2) lack/loss of response, and 3) adverse events (AEs) were assessed using Kaplan-Meier survival to compare patients 1) with and without MTX use; 2) with or without prior biologic use at initiation of TOFA was assessed using Kaplan-Meier survival analysis. Cox proportional hazards regression model was also used to assess TOFA discontinuation adjusting for propensity score to balance the two treatment groups.

Results: Among the 131 patients, 70 (53.4%) received TOFA without MTX and 61 (46.6%) TOFA with MTX. Mean (SD) age and disease duration were 60.2 (9.8) years and 13.7 (9.3) years, respectively. The majority were females (89.3%) and most had prior biologic use history (74.0%). Discontinuation was reported in 44 (33.6%) of all TOFA patients with a median survival of 31.3 months. Overall retention of TOFA at 6, 12 and 24 months was 80.5%, 63.1% and 53.5% respectively. These findings are very similar to the results reported from the RHUMADATA registry at ACR 2018. Fifteen (34.0%) patients stopped their TOFA due to non-response/loss of response, 22 (50.0%) due to adverse events, and 7 (16%) due to other reasons. Discontinuation due to any reason was borderline significantly lower in the TOFA with MTX group compared with TOFA without MTX group. There was no significant difference in TOFA discontinuation between the two groups of patients with and without prior biologic use (Logrank p=0.77).

Conclusions: We found that half of the RA patients remained on TOFA 31 months after initiation. TOFA retention is similar between patients with and without MTX group specifically for lack/loss of response or adverse events reasons. However, the interpretation of results is limited because of small sample size. Merging data with other RA registries in Canada is proposed to increase study power and to provide more robust results.

10. Adherence and risk factors for stopping treatment in a cohort of Quebec patients newly initiated on statins (OBSTAT cohort)

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Background: Despite the demonstrated effectiveness of statins in reducing risk of cardiovascular events in high-risk patients, adherence to treatment remains a barrier.

Objectives: To describe adherence of patients newly initiated on a statin, and identify potential risk factors for stopping treatment.

Methods: Patients newly initiating statin therapy in Montreal, Chicoutimi or Quebec City were invited to participate in this prospective cohort study. At baseline, eligible participants completed questionnaires detailing their personal and familial medical histories, context for statin initiation, lifestyle habits, and biological parameters. Patients were followed at 1, 3, 6, 9, 12, 18, and 24 months where treatment continuation status and potential side effects were recorded. Adherence was defined as taking statins during at least 80% of follow-up. Multivariate cox regression with forward selection was used to identify potential risk factors for stopping treatment.

Results: 1,631 new statin-users were enrolled (mean age 57.4 years, 47.6% women, mean follow-up time 706.8 days). 33.6% of patients stopped treatment at least once during follow-up. 74.3% of patients were considered adherent. Statistically significant risk factors for stopping therapy were as follows: history of pain (HR=1.43), switching statins (HR=1.84), mention of potential adverse effects by their physician (HR=1.22), family history of cardiovascular risk (HR=0.64), male gender (HR=0.73), perceiving controlling cholesterol as important (HR=0.49), and living outside Montreal (HRQuebec=0.49, HRChicoutimi=0.81).

Conclusions: Almost three quarters of patients were adherent to treatment. Those who switched statins, had been made aware of potential adverse effects, or who had a history of pain were more likely to stop treatment.

11. Influence of opioid prescribing standards on health outcomes among patients with chronic opioid use: a longitudinal cohort study

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Background: The introduction of College of Physicians and Surgeons of British Columbia opioid prescribing standards and guidelines in mid-2016 was associated with reduced opioid analgesic use among patients with chronic use of prescription opioids in British Columbia. In this study, we evaluated the impact of the standards and guidelines on health outcomes.

Methods: We conducted a longitudinal cohort study using administrative data. The study included BC patients with chronic use of prescription opioids, excluding those with a history of long-term care, palliative care or cancer. We followed patients for a 12-month pre-policy period and 10-month post-policy period. We evaluated level and trend (slope) changes in rates of opioid overdose hospitalization, and secondary outcomes of all-cause hospitalizations, all-cause emergency room (ER) visits, opioid overdose mortality, and all-cause mortality.

Results: The study included 68,113 patients in the main cohort and 68,429 historical controls. We found no impact on opioid overdose hospitalizations in level (adjusted rate ratio 0.83; 95% CI 0.45 to 1.54) or in trend (adjusted RR 1.00; 95% CI 0.91 to 1.10). All-cause hospitalizations declined in level but increased in trend, reflecting a temporary decrease in hospitalizations. We found no significant changes in all-cause ER visits, opioid overdose mortality, or all-cause mortality.

Conclusions: Among patients with a history of chronic prescription opioid use, we did not find a clear association between the prescribing standards and guidelines and opioid overdose hospitalizations, all-cause ER visits, opioid overdose mortality, or all-cause mortality, or a sustained reduction in all-cause hospitalizations, over a 10-month post-introduction period.

12. Cost-utility analysis of electroconvulsive therapy and repetitive transcranial magnetic stimulation for treatment-resistant depression in Ontario

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Objectives: To evaluate the cost-effectiveness of rTMS (repetitive transcranial magnetic stimulation) and ECT (electroconvulsive therapy) in patients with treatment-resistant depression (TRD) in Ontario.

Methods: A cost-utility analysis evaluated the lifetime costs and benefits to society of rTMS and ECT as first-line treatments for TRD using a Markov model. Treatment efficacy and health utility data were extracted and synthesized from randomized controlled trials and meta-analyses evaluating these techniques. Direct costing data were obtained from national and provincial costing databases. Indirect costs were derived from government records. The annual discount rate was 1.5%. Scenario, threshold and probabilistic sensitivity analyses were performed to test robustness of the results.

Results: rTMS dominated ECT in the base case scenario. rTMS patients gained an average of 1.2 additional quality-adjusted life years (QALYs) with lifetime costs that were $76,164 less than ECT. rTMS remained dominant in all sensitivity and scenario analyses, except for one scenario in which the maximum lifetime allowance of rTMS acute phase treatments was reduced to match that of ECT. In this scenario rTMS produced average lifetime cost savings of $40,474 but was marginally less effective than ECT (<0.1 fewer QALYs gained).

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Conclusion: From a societal perspective utilizing a lifetime horizon, rTMS is a cost-effective first-line treatment option for TRD relative to ECT. The reduced side effect profile and increased patient acceptability of rTMS that allow it to be administered more times than ECT in a patient's lifetime may contribute to its cost-effectiveness.

13. Journey to stability with psoriasis: key findings from a national survey

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Purpose: Finding a treatment that works and achieving a satisfactory level of symptom stability can be an ongoing and onerous process for some people with psoriasis. Recognizing this, the Canadian Psoriasis Network and the Canadian Association of Psoriasis Patients collaborated on a survey of Canadians with psoriasis to better understand what this journey looks like. Stability was defined as an individual's personal comfort with the effectiveness of treatment, the degree of skin clearance and quality of life. Survey results reinforce the notion that achieving stability can be a burdensome process, involving trying several medications before finding one(s) that is effective for the individual. Decreasing barriers to diagnosis and treatment, increasing education about treatment options and preserving shared-decision making between patients and their treating clinicians are some ways that the health system, health providers and patient organizations can better respond to the needs of patients with psoriasis.

Methods: The Journey to Stability survey was open from September 15 to November 8, 2017. Online surveys were completed by 286 English and 36 French respondents, with the majority (96.5%) being adults living with psoriasis. Most respondents identified as having either moderate (41.96%) or severe (28.67%) symptoms.

Results: The majority of respondents have lived with psoriasis for 20+ years. A large number (38%) feel that their condition was not satisfactorily controlled for 10+ years and 24% indicated that they are still not stable. Most respondents (80.35%) indicated that psoriasis negatively affected their daily lives to some extent. Treatment trial and error, wait times for dermatologist appointments and gaps in knowledge about treatments emerged as potential barriers to achieving stability.

Discussion: Survey findings suggest that living with uncontrolled psoriasis can contribute to poor self-esteem, loss of sleep, anxiety, depression, missed work days and intimacy avoidance. Delays in seeing a dermatologist, treatment trial and error and gaps in knowledge about treatments, like biologics and biosimilars emerged as potential barriers to achieving stability. Access to timely diagnosis and treatment options (including prescription medications and light therapy) is essential for people to find treatment that works for them and to ensure that people have other options should their medication no longer work for them. Treatment decisions are often difficult and emotional. When respondents changed medications because they were not effective, the majority (65.32%) reported being negatively affected. Without education and without informed decision-making with their treating clinician, people who are stable after a lengthy and emotional journey reacted strongly to the possibility of being switched to another medication for non-medical reasons. Any therapeutic changes require education and a good decision-making process with providers to assess best outcomes. A positive finding is that the majority of respondents appear to value their relationship with their treating clinician, with 73.4% reporting that they have a part in treatment decisions. The vast majority (90.17%) indicated that they were comfortable discussing any dissatisfaction with medication with their physician.

14. A prospective observational study on quality of life (QOL) among dispatchers and call takers in the emergency paramedic unit in Greater Vancouver Area

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J Popul Ther Clin Pharmacol Vol 26(3):e14–e34; October 18, 2019

Dispatchers and Call Takers are among the most highly skilled of Emergency Medical Services who deal with the medical emergencies outside of a hospital. Paramedical Staff is a healthcare professional concerned with pre hospital set up, medical care intended for the people and out of hospital environment. In Canada these are the people who work either on land ambulances or air ambulances with a valid license issued by Provincial authorities. Paramedical Staff witness their patients, clients at their worst conditions, demonstrating long lasting effects resulting in depression. Ironically, they are most often ignored. Their job is thankless as they deal with the people at their time of distress. The study will be a cross sectional prospective observational study carried out among a sample size of 100 in and around Greater Vancouver Area (GVA) among paramedical staff, to obtain an insight pertaining to Socioeconomics, demographics, lifestyle factors, behavioural changes and health related quality of life (HRQoL) using EuroQol EQ-5D-5L. A questionnaire is framed comprising of almost 35 questions revolving around the above mentioned criteria. Ethical consent will be obtained from Ambulance Paramedics of BC (APBC). Data analysis will be done using SPSS version 16.0. The data will be analysed to determine the factors affecting the quality of lives of the paramedics and suitable recommendations would be given to overcome the hardships along with unfolding of any knowledge gap existence. This is the first study of its own kind and is intended to be published in a High Impact Factor Journal.

15. Penultimate revised version of the Patented Medicine Prices Review Board (PMPRB) pharmaceutical budget impact analysis (BIA) guidelines

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Introduction: Following the generation of a proposal for updating the 2007 Patented Medicine Prices Review Board (PMPRB) pharmaceutical budget impact analysis (BIA) guidelines we assessed the degree of discordance between the old and the new (proposed) guidelines.

Methods: A list of BIA recommendations was developed based on discordance between the PMPRB 2007 BIA guidelines recommendations and fifteen Canadian (federal, provincial and private payers) and other national and transnational BIA guidelines worldwide published since 2007. Through a mixed methods study, Canadian stakeholders' feedback were obtained on the proposed list of BIA recommendations and ultimately a proposal for updating PMPRB BIA guidelines was finalized.

Results: The proposal consists of 72 recommendations, of which 49% (n=35) are identical with the PMPRB 2007 BIA guidelines (e.g., inclusion of off-label indications in the sensitivity analysis, considering market/clinical data from other jurisdictions and expert opinions as acceptable sources of data and not including cost offsets and indirect costs), thirty-six percent of recommendations (n=26) are new (e.g., catch-up effect, dynamic population, scenario analysis and reporting gross and net impact), and the remainder (15%; n=11) are modified from the original version (e.g., time horizon, health care resource utilization and modelling).

Conclusions: The analysis demonstrates that the 2007 guidelines are outdated and need significant revision. This penultimate version addresses the limitation of the older version but still requires a broader consultation among stakeholders prior to a final revision and approval. Further Canadian stakeholder feedback is required for reaching consensus on inconclusive recommendations.

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17. Enhancing medication adherence through an adherence support program

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Objectives: To evaluate whether patients who receive systematic adherence phone calls from an Adherence Support (AS) program achieve better medication adherence than a matched control group of patients. This AS program is a HealthForward service provided on behalf of Green Shield Canada (GSC) and implemented as an enhanced service which focuses on adherence support for GSC plan members.
Methods: During the identification period (October 2015 through September 2016), GSC pharmacy claims data from the following two cohorts were compared - A) Patients who received adherence support through the AS program (intervention group); B) Patients who did not participate in the AS program (control group). Medication adherence was measured by modified medication possession ratio (mMPR).
Results: The final claims data for analysis consisted of 79 AS program patients who were able to be matched with 331 control patients. The top 3 (out of 11) disease conditions amongst these patients were rheumatoid arthritis, Crohns/ulcerative colitis, and psoriasis. AS program patients demonstrated higher medication adherence than control patients after matching the cohorts on 4 variables - drug, disease condition, gender, and age group (mMPR: 95.2% vs. 93.8%; p=0.002). The percentage of patients who met the mMPR threshold of 90% was also higher in the AS program patients compared to control patients (73.8% vs. 49.2%; p=0.004).
Conclusions: The analysis demonstrates that AS program patients benefit from enhanced medication adherence. Further research is needed to understand whether this difference in adherence is clinically meaningful.

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18. Comparing manufacturers and CADTH economic evaluations of anti-cancer drugs

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Background: Anti-cancer treatments undergo a health technology assessment by the Canadian Association for Drugs and Technologies in Health (CADTH), evaluating both clinical and economic factors to provide reimbursement recommendations to provincial payers. Manufacturers submit estimates of quality-adjusted life years (QALYs) gained, and incremental cost-effectiveness ratios (ICERs). CADTH's Economic Guidance Panel (EGP) will conduct a re-analysis of these metrics. This analysis identifies and compares trends in estimates from both groups.
Methods: QALY and ICER values were retrieved from final reimbursement recommendations available as of May 31, 2019. Only data from products that received a positive recommendation were included in the primary analysis. Conservatively, EGP lower-bound QALY and upper-bound ICER values were used. Linear regression analysis was conducted to determine the average annual changes.
Results: For manufacturer-submitted estimates, the average annual change in efficacy improvements was 0.171 QALYs gained per year (95% CI, 0.076-0.267), and average annual change in cost-effectiveness was $2,943/QALY (95% CI, -$4,263-$10,122). The EGP-reassessed values saw average annual incremental QALYs decreasing by 0.110 (95% CI, 0.037-0.183), and worsening cost-effectiveness by $8,927/QALY (95% CI, -$10,371-$28,226). In a pairwise comparison, the average difference between manufacturer-submitted and EGP-reassessed QALYs was a decrease of 0.486 (-49%), and an increase in ICERs of $138,557/QALY (+54%).
Conclusions: The increase in QALY values shows that clinical efficacy of anti-cancer treatments has improved despite worst-case EGP-reassessed estimates, and the slight increase in ICERs shows that the increase in innovation had only a minor impact on cost-effectiveness of drugs.

19. Confounding adjustment in observational economic evaluations needs to be improved, a systematic review

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Background: Observational economic evaluations (i.e., economic evaluations based solely on observational data) are prone to confounding bias. Prior studies have shown that adjusting for confounding is poorly done, if done at all, in these studies. Although recent knowledge translation efforts have tried to highlight these issues, it is unclear what their impact has been. We therefore aimed to investigate whether and how confounding is accounted for in observational economic evaluations in Cardiology.
Methods: We performed a systematic review of PubMed, Embase, Cochrane Library, Web of Science and PsycInfo databases using a set of Medical Subject Headings and keywords covering topics in Observational Economic Evaluations in Health and Cardiovascular Diseases. Any study published between January 1st 2013 and December 31st 2017 addressing our search criteria was eligible for inclusion; no other exclusion criterion was imposed. We screened all eligible reports to identify which confounding adjustment method was used. Our protocol was registered with PROSPERO (CRD42018112391).
Results: A total of 8,771 unique citations were screened, with 40 publications selected for full text extraction. Less than half of the selected studies adjusted for confounding bias (n=19 [47.5%]). Of the various confounding adjustment methods available, matching was favored in 15 of the 19 studies.
Conclusion: Despite previous efforts, our results indicate that adjustment for confounding bias remains poorly done in observational economic evaluations.

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Such results support continued knowledge translation efforts aimed at improving researchers knowledge and skills regarding confounding bias and methods aimed at addressing this issue.

20. Early insight into new medicine launches in international markets

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New medicines are a fast-growing segment of the Canadian market, with those launched between 2009 and 2017 accounting for over a third of all pharmaceutical sales by the end of 2018. High-cost specialty medicines have an increasingly important impact on this growth, as many new biologic, orphan, and oncology products have treatment costs in tens or hundreds of thousands of dollars per year, yet many have limited evidence of therapeutic benefit. This study explores the market entry dynamics of new medicines launched in Canada and internationally. The presentation explores the availability, pricing, uptake, and sales of medicines launched in 2017 and provides a preliminary analysis of launches in 2018, with a focus on recent entries to the Canadian market. The international markets examined include the seven PMPRB comparator countries as well as other countries in the Organisation for Economic Co-operation and Development (OECD). Results are based on information from the FDA, the EMA, and Health Canada, as well as IQVIAs MIDAS Database. Canada launches more new medicines than most OECD countries but fewer than the PMPRB7 comparators, many of which have lower average patented medicine prices. However, Canada ranks high for its share of corresponding new medicine sales, suggesting that the higher-selling medicines are available. The share of orphan drugs among new launches jumped to 59% in 2018, continuing the steep climb observed in recent years. This presentation provides decision makers, researchers, and patients with important information on emerging therapies in the Canadian and international pharmaceutical environment.

21. The efficacy of pharmaceutical cannabinoids in the management of cannabis use disorder: A systematic review.

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Background: Cannabis use disorder has become a concern as a result of increased availability of cannabis and reduced perceived risk of harm. The use of psychosocial interventions is associated with high rates of relapse, suggesting a possible need for pharmacotherapy. Cannabinoid replacement therapy with pharmaceutical cannabinoid agents is a possible therapeutic option.
Methods: In August 2018, we searched MEDLINE, EMBASE, IPA, and the Cochrane library Databases, for randomized controlled trials that compared the use of a pharmaceutical cannabinoid agent with placebo or other interventions for the management of cannabis use disorder. Data were extracted using a standardized form and risk of bias across studies was assessed using the Cochrane tool. Withdrawal was measured using standardized mean differences after adjusting all scores to 1-100 scale and we assessed abstinence using a random-effects model. Results were meta-analyzed using Revman 5.3.
Results: Out of 486 reports identified, this review included six trials with a total of 403 participants and the duration of treatment ranged from 6 days to 12 weeks. All trials showed no statistical difference between pharmaceutical cannabinoids or placebo in abstinence rates (OR= 1.13; 95% CI: 0.65, 1.95, in favour of placebo) or decreasing cannabis

withdrawal symptoms (standardized mean difference in withdrawal scores -0.14; 95% CI: -0.57, 0.29, in favour of cannabinoids). Three of the trials were at high risk of bias.
Conclusion: The currently available evidence does not support the use of pharmaceutical cannabinoids for cannabis use disorder management.

22. The impact of patented drug price controls on drug launches: evidence from the OECD countries

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Background: Canada's Patented Medicine Prices Review Board (PMPRB) regulates the introductory prices of patented drugs and their rate of increase over time. The PMPRB has been criticized because prescription drug prices in Canada are relatively high. In response, the PMPRB has proposed major changes to the way that it regulates drug prices. A cost benefit analysis (CBA) conducted by the Government of Canada concluded that these changes would lower drug prices and benefit Canadians. However, the CBA ignored several costs to Canada from reducing rx drug prices. The literature indicates that lower drug prices will likely delay the launch of new drugs into Canada. In this study, we attempted to estimate how lower drug prices will affect new drug availability in Canada.
Methods: Seven multiple variable linear regressions were estimated to assess the impact that price, population, population served by the regulatory body, and GDP per capita have on drug availability across 31 OECD countries. The model estimates were utilized to predict the impact of a price decrease on drug availability in Canada.
Results: Multi-year model estimates showed that, holding all other variables constant, a 25% decrease in patented drug prices in Canada from 2009-2016 (7 years) would have resulted in a 6% decrease in drug availability. Single year model estimates showed the same price decrease between 2016-2017 would result in a 9% decrease in drug availability.
Conclusion: This study highlights a flawed assumption in the Government of Canada's assessment of the costs of the proposed PMPRB changes. Price is an important variable upon which drug launch is dependent across OECD countries. A comprehensive analysis of the desirability of the proposed PMPRB policy changes thus needs to account for the cost to drug payers and patients from the reduced access to new drugs.

23. Real-world Persistence with Plegridy versus Rebif for the Treatment of Multiple Sclerosis in Canada

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Objectives: Persistence with disease-modifying therapies is associated with fewer relapses and hospitalizations, which can reduce healthcare costs among patients with multiple sclerosis (MS). We quantified the persistence of first-line, subcutaneous injectable peginterferon beta-1a (Plegridy®, peg-IFNß-1a) to more frequently dosed subcutaneous injectable interferon beta-1a (Rebif®, IFNß-1a), among Canadians with relapsing-remitting MS.
Methods: A retrospective claims analysis was conducted based in part on information provided by IQVIA Solutions Canada Inc. All rights reserved. We identified Canadians who initiated peg-IFNß-1a or IFNß-1a, between 2015/12 and 2017/06. Patients with no MS drug claims ≤24 months of initiation were included and followed for 12 months from first dispensation. Persistence, defined as continuous treatment with no interruption >35 days, was estimated using Kaplan-Meier curves. Cox proportion hazards models adjusted for demographic covariates, and assessed the relative risk of discontinuation.
Results: A total of 120 patients (71.7% female; mean age=43.4 years) initiated peg-IFNß-1a (n=36) or IFNß-1a (n=84). Mean treatment duration was 307.5 (SD=93.7) days for peg-IFNß-1a and 252.0 (SD=122.8) days for IFNÎ²-1a. At 12 months, 46.4% of IFNß-1a-treated-patients remained on

therapy versus 65.7% of peg-IFNß-1a-treated-patients. Patients who initiated IFNß-1a had a significantly greater risk of discontinuation, compared to peg-IFNß-1a (HR=2.06; 95% CI=1.1-3.9; p=0.03).
Conclusion: Persistence with peg-IFNß-1a was higher than IFNß-1a. We (the authors) believe this may be attributable to its less frequent dosing regimen. However, further research with a higher sample size is needed. Medication persistence should be considered when selecting MS therapies for coverage and treatment, since continuous drug exposure can improve clinical outcomes.

24. Improved health outcomes in patients receiving health case management (HCM)

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Background: To demonstrate that health case management (HCM) administered with routine care (RC) delivers better health outcomes than RC alone. HCM is a Great-West Life program aimed at monitoring health outcomes and managing costs of certain specialty drugs.
Methods: Data from two HCM cohorts i) Rheumatoid arthritis (RA) patients on adalimumab, and ii) Psoriatic arthritis (PsA) patients receiving etanercept, were compared to published real-world observational data of Canadian RA and PsA patients treated with these therapies respectively. Two published studies were identified for comparison with HCM RA on adalimumab: Study 1-NCT01585064 and Study 2-NCT01117480. HCM PsA on etanercept was compared with Study 3 NCT00127842.
Results: Between June 2012 to Dec 2016, 99 RA and 31 PsA HCM patients were eligible for data analysis. In RA patients on adalimumab, unadjusted comparisons demonstrated higher reduction in HAQ-DI score over 6 months in HCM compared to RC [0.97 vs. 0.47(study 1), p<0.001 and 0.97 vs. 0.31(study 2), p<0.001]. The percentage of patients achieving low disease activity (LDA) after 6 months was higher in HCM than RC [54.1% vs. 28.4% (study 1), p=0.005]. Similarly, percentage of patients achieving remission after 6 months was higher in HCM than RC [45.9% vs. 17.4% (study 1), p=0.001 and 45.9% vs. 13.0% (study 2), p<0.001]. In PsA patients on etanercept, a higher percentage of HCM patients achieved HAQ-DI reductions of 0.5 points after 6 months compared to RC [84% vs. 62%(study 3), p=0.025].
Conclusions: This analysis demonstrates the benefit of HCM in improving health outcomes over RC alone, and helps inform future HCM prospective studies.

25. A case study of the proposed amendments to patent medicine review prices regulations in Canada

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Background: Drug expenditures are increasing worldwide, with spending largely driven by the entrance of high-cost specialty drugs to market. In response to growing concerns about drugs costs and the sustainability of healthcare systems, attention is turning to reducing drug prices to manage expenditures. The Patented Medicine Prices Review Board (PMPRB) is engaged in a process to modernize the regulations governing patented medicine prices in Canada. A significant addition in these reforms is the use of pharmacoeconomic analyses to set price ceilings of new medicines. This new price control factor may have a disproportionate effect on orphan drugs.
Methods: The objective of this policy analysis was to estimate the impact of the proposed PMPRB amendments on orphan drug prices. Following the methods detailed by PMPRB in recent publications, Pharmacoeconomic Value (PV) ceiling prices were calculated for orphan drugs approved in 2017 CADTH

reviews, where available. Willingness-to-pay (WTP) thresholds of $180K/QALY, $120K/QALY, and $60K/QALY were used.

Results: Of the 16 orphan drugs approved by Health Canada in 2017, 12 were reviewed by CADTH. 6 of these reviews could be utilized to calculate a PV price. 2 of these products were considered cost effective at the submitted price. For the remaining 4 products, PMRPB would require average price reductions of 75%, 83%, and 91% using the three specified WTP thresholds.

Conclusions: There exists a substantial gap between the original price and the potential price under the proposed PMPRB regulatory changes, which could put future orphan drug launches at risk.

26. Evaluation of drug treatment awareness, prescription patterns and adverse drug reactions in patients with schizophrenia

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Introduction: Medication awareness is an important factor that ensures adherence among patients with Schizophrenia. Knowing the particular lacunae in the awareness of treatment is of due importance so as to develop specific measures towards this domain. In this study, authors decided to study drug awareness, prescription patterns and adverse drug reaction profile in Schizophrenia patients.

Methodology: After obtaining IEC permission, eligible patients and their caregivers were recruited in this cross-sectional, observational study. Data about drug awareness among patients was obtained using a self-designed validated questionnaire consisting of 16 items. Drug awareness was also checked in caregivers of these patients. Information about antipsychotic medications and changes in medications over the last 3 months were reviewed. ADR evaluation in terms of causality (WHO UMC scale), severity (Hartwig Siegel scale) and preventability (Schumock and Thornton scale) was done.

Results: 250 patients and 150 caregivers between the age of 18-65 years were included in the study. More than 65 % of the patients had good insight. Of these >60% were aware about the details of their current prescription, almost 90 % were aware about the importance of doctor-patient interaction, while only about 50 % of them knew about the side effects of the medications prescribed. Second generation antipsychotics (Risperidone and Olanzapine) were the most commonly prescribed. Sedation was the most common ADR and majority of the ADRs were mild, not preventable.

Conclusion: Patients with Schizophrenia and their caregivers should be counselled adequately to ensure medication awareness which will thereby help to increase medication adherence among patients.

27. Health system cost for cancer medications and radiation treatment in the four most common cancers

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Objective: This analysis calculated the mean overall cost per patient per cancer-related medication (CRM) and radiation treatment (RT) by disease and stage in the first year (365 days) after diagnosis.

Methods: A retrospective cohort study design was used to identify population health system resources and costs for patients diagnosed with breast, colorectal cancer, lung and prostate cancer between January 1, 2010 and December 31, 2015. The overall average cost per patient in 365 days after diagnosis was determined for cancer-related medications and RT using two costing algorithms. The cost by disease subtype and stage were determined.

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Results: There were 168,316 Ontarians diagnosed with breast (N=50,141), colorectal (N=38,108), lung (N=34,809) and prostate (N=45,258) cancer. CRM overall mean (95%CI) costs were $8,167 (8,023-8,311); $6,568 (6,446-6,691); $2,900 (2,816-2,984); and $1,211 (1,175-1,247) for breast, CRC, lung and prostate respectively. Mean overall RT costs were $18,529 (18,415-18,643); $15,177 (14,899-15,456); $10,818 (10,669-10,966); and $16,887 (16,648-17,125). Stage III and IV were the most expensive across four cancers for CRM and RT.
Conclusions: Previous costing and resource estimates have not been robust because of the lack of comprehensive data on CRM and RT. This work updates previous costing estimates to understand resources and costs critical to health system planning in a single payer system.

28. Assessment of recent HTA recommendations for RWE opportunities

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After many years of discussion, the Canadian environment now seems primed to decide the role that RWE will play in the pharmaceutical system. In October 2018, CAPT, IHE, Health Canada (HC), and CADTH hosted a workshop entitled Defining Decision-Grade Real-World Evidence and its Role in the Canadian Context: A Design Sprint with the goal of identifying the value and application of RWE in supporting pharmaceutical regulatory and reimbursement decision-making; and, identifying the conditions upon which RWE will be considered of sufficient quality to inform decision-making. Subsequently, HC and CADTH started the development of a joint framework for the integration of RWE into regulatory and reimbursement decision-making in Canada.

There have been several recent CADTH and INESSS HTA recommendations which have included direction to undertake RWE generation. The challenge for decision makers is to translate these recommendations into practical approaches to meet their needs as they strive to make informed decisions on product funding. A case series of recent CADTH and INESSS HTA recommendations (January 2018 to June 2019) was evaluated to examine trends, commonalities, and other key insights that would impact the implementation of an RWE strategy to support patient access. Based on this analysis, suggestions for potential RWE approaches were developed for each scenario. These initial suggestions were validated with several decision makers, and their feedback has been included in the analysis. The suggestions emanating from this project should be considered as HC and CADTH continue to develop their RWE framework.

29. Is Canada's data infrastructure ready for value-based agreements?

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Background: Breakthroughs in biopharmaceutical research are ushering in a life-changing era of precision medicine that is truly patient focused. Payers and health system administrators are concerned with budget sustainability and evidence gaps which need to be addressed with the manufacturer prior to reimbursement. It is often the case that data from the randomized clinical trial programs, appropriate for regulatory approval, does not meet the evidentiary needs of payers. In Canada's current sequential system of drug approval, evaluation and funding, this delays or denies patient access to these new medicines. Paramount to funding is generating real world evidence (RWE) on the value these precision medicines bring to patients and the healthcare system as a whole. If RWE is to be generated in support of value-based agreements (VBAs), Canada requires a supportive data infrastructure. The objective of this research is to assess Canada's data readiness for value-based agreements.
Methods: The feasibility of VBAs in Canada will be explored in three ways: 1) through literature reviews

of data requirements of VBAs in other markets for reimbursement and patient access decision making; 2) direct, confidential, interviews with key Canadian stakeholders such as payers, data institutions, patient advocates, clinicians, healthcare leaders; 3) survey of data systems in existence and their readiness as well as accessibility for VBAs. Specifically, research questions will focus on: 1) data requirements (including acceptability of proxies) for reimbursement decision making, and 2) charting a roadmap for stakeholders to partner on various VBA constructs, including acceptable complexity trade-offs, to facilitate successful agreements.

Results: A sentinel assessment of available data sources along with health system readiness across Canada will be undertaken, assessing data elements captured as well as their accessibility to both industry and government for use in value-based agreements.

Conclusions: Overcoming the inertia of vested interests in healthcare system funding, budgeting and decision making will be critical to improving patient care and health system value for innovative medicines. VBA constructs such as subscription model, mortgage model, or indication-based pricing could meaningfully improve patient care and health system value, despite their added complexity relative to the current first dollar discounts common in Canadian product listing agreements (PLAs). All stakeholders have an important role to play in data generation and stewardship, improving patient care, and delivering the full value of medicines. The question remains: is Canada's data infrastructure ready for value-based agreements?

30. Comparative analysis of stakeholder views on proposals for updating the Patented Medicine Prices Review Board (PMPRB) Budget Impact Analysis guidelines: public or private payer versus industry perspectives

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Introduction
The present study was designed for obtaining Canadian pricing and reimbursement stakeholders' opinion on a list of proposed recommendations for updating the 2007 Patented Medicine Prices Review Board (PMPRB) Budget Impact Analysis guidelines.

Methods: Stakeholders from different perspectives including policymakers (public and private payers) and industry experts/consultants were invited to participate in the study (private payer and industry perspectives were not included in the PMPRB 2007 BIA guidelines). Using a mixed methods approach, an interview guide and a written survey were developed based on discordance between the PMPRB 2007 BIA guidelines recommendations and Canadian provincial, and other national or transnational BIA guidelines. A thematic content analysis was applied for the qualitative data analysis.

Results: We conducted nine interviews with policymakers and twenty-seven surveys with industry experts/consultants. Most interviewees were positive about the usefulness of BIA in disinvestment decisions and believed that reviewing cost-effectiveness analysis (CEA) and BIA together, at the same time, could be particularly informative for setting value-based prices. Fifty-six percent of the proposed recommendations were approved (e.g., the use of post-market real-world data for assessing the reliability of BIAs first-year forecasts), whereas, 30% were not supported by stakeholders (e.g., indirect costs). Some recommendations will need further input from public and private payers before being included in a revised version of the PMPRB BIA guidelines (e.g., inclusion of cost offsets).

Conclusions: In the present study, Canadian payers and manufacturers' views on the BIA recommendations, obtained through qualitative and quantitative methods, provide additional insight to help define BIA guidelines from a Canadian perspective. This information may also be of value for updating or creating BIA guidelines worldwide.

31. Biosimilars in Canada: current environment and future opportunity

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Patented Medicine Prices Review Board (PMPRB)

Potential savings from biosimilars is a subject of keen interest to Canadians, especially in light of the patent life extensions for biologics negotiated in the recent USMCA. Biosimilars offer an opportunity for significant cost reductions, as our annual national sales for biologics tops $7 billion, or over 40% of all patented medicine sales.

While the international experience has many success stories, marked by early biosimilar entry, healthy competition amongst the manufacturers, and sizable discounts and uptake, domestically the market dynamics have been less encouraging. In Canada, biosimilar uptake and approval rates, as well as competition among biosimilars, lags well behind Europe. For example, in the last quarter of 2017, the uptake for infliximab biosimilars in Canada was only 4%, compared to a median of 34.5% for the OECD.

Capturing data from various sources, including the IQVIA MIDAS™ Database, the FDA, EMA, and Health Canada, and GlobalData, this presentation compares the overall emerging Canadian market for biosimilars with our international counterparts. The analysis delves more deeply into the uptake, pricing, and the cost implications, for specific biosimilars, with a focus on the public drug plans. It also provides a glimpse into emerging biosimilar medicines in the pipeline.

As the historic savings from generic price reductions and substitutions begin to wane, the potential savings from biosimilars could play in increasing role in offsetting rising drug costs. This overview will uncover the current gaps as well as the potential savings from aligning the Canadian uptake and pricing of biosimilars with other industrialized countries.

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