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1

Fiscal Cost-Benefit Analysis of Antiretroviral Therapy for the Management and Prevention of Human Immunodeficiency Virus (HIV) in Canada 1987-2021

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Background: Since the introduction of antiretroviral therapy (ART) in 1987, governments and health services have been investing to reduce disease transmission and improve the lives of people living with HIV (PLWHIV). This cost-benefit analysis aims to quantify the fiscal return of investment in ART from the perspective of the Canadian government over the 1987-2021 period.

Method: Historical data for ART-preventable mortality, morbidity, and incident cases were compared with a scenario without ART funding, constructed using time series analysis and transmission dynamics. Reductions of AIDS cases, deaths, and incident HIV infections, resulting from ART, were converted into averted loss of lifetime tax revenue, and avoided lifetime healthcare costs. The effects on lifetime employment insurance costs for PLWHIV along with the impact of ART-induced longevity on long-term governmental expenditures were also quantified.

Results: Investing in ART yielded $28.7-billion in avoided healthcare costs and $47.1 billion in averted tax revenue loss. Spending on employment insurance for PLWHIV increased by $0.28 billion. Without the fiscal effect of longevity, the estimated benefit-cost ratio (BCR) was 5.91. The BCR remained favorable when the fiscal effects of longevity were considered. Despite additional fiscal expenditures, including $13.5-billion in old-age benefits, $14.2-billion in disability benefits, and $7.9-billion in non-HIV related healthcare costs, the estimated BCR was $3.09.

Conclusions: The Canadian government has generated significant fiscal returns from investing in ART; for every $1 invested, investment in ART has produced $3.09 and $5.91 in fiscal benefits with and without the inclusion of longevity's fiscal costs, respectively.

2

Comparing approaches to determine the costs of treating burn victims in Quebec

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Background: Quebec's healthcare system is transitioning from a fixed-budget financing to one based on the volume of care provided. This funding is initially based on an indicator of the level of resources used (NIRRU), equivalent to the resource intensity weights used elsewhere in Canada. This funding will soon be derived from a newly implemented real cost database: CPSS (Coût par parcours de soins et de services). We assume that the measurement of burn treatment costs will vary according to the method employed. The objective of this research project is to evaluate and compare the costs of care for adult patients admitted to the burn unit of the CHU de Québec-Université Laval during their index hospitalization, i.e. the first hospitalization following a burn, according to these two methods.

Methods: A retrospective study of medico-administrative and economic data was conducted. Target patients were admitted to the burn unit between April 1, 2017, and March 31, 2021. Index hospitalization costs were obtained using the i) NIRRU and ii) CPSS costs. Average costs stratified by patient characteristics were estimated and comparative analyses of the two measures were performed with paired t-tests and Spearman's correlation coefficient.

Results: Our cohort comprised 362 patients. The total direct cost of the cohort measured by the NIRRU was $5,517,162, compared with $9,548,459 obtained using the CPSS. A spearman correlation coefficient of 0.9 ($p<0.001$) was obtained.

Conclusion: These methods of calculating costs show a significant discrepancy. However, it is impossible to determine which measure is the most valid.

3

Extended-release prescription opioids and risk of HCV infection among people who inject drugs: Findings from the HEPCO cohort in Montreal, Quebec, Canada

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Background: People who inject drugs (PWID) are at high risk of hepatitis C (HCV) infection. Prescription opioid (PO) injection appears to increase HCV risk relative to heroin injection, but the impact of PO dosage release formulation (immediate vs. extended-release) remains unclear.

Objective: To compare HCV incidence among PWID injecting different types of opioids in Montreal.

Methods: Data were from the Montreal Hepatitis Cohort (HEPCO) of PWID (2011-2020). HCV RNA-negative participants completed interviewer-administered questionnaires and blood sampling every three months. Self-reported past-month opioid injection was categorized into no opioid injection, heroin injection (without PO injection), extended-release PO injection, and other PO injection. Multivariate time-dependent Cox regression (adjusting for biological sex, age, and calendar year) estimated adjusted Hazard Ratios (aHR) for time to new HCV infection.

Results: Of 809 cohort participants, 580 HCV RNA-negative people (82% male, median age 40) contributed 5465 visits across 1861 person-years of follow-up. Overall, 134 acquired HCV for an incidence of 7.2 per 100 person-years. Crude HCV incidence (per 100 person-years) across categories was: no opioid injection 3.6 (95%CI 2.6-4.8), heroin injection 3.3 (95%CI 1.6-6.1), any extended-release opioid injection 16.3 (95%CI 4.1-44.3), and other prescription opioid injection 21.1 (95%CI 16.9-26.2). Compared with no opioid injection, risk of HCV infection was elevated among people injecting extended-release PO (aHR 3.5, 95% CI 1.1-11.2) or other PO (aHR 4.6, 95%CI 3.0-6.8) but not heroin (aHR 0.92, 95%CI 0.44-1.94).

Conclusions: Among PWID in Montreal, HCV risk is elevated when injecting prescription opioids and differs little between immediate- and extended-release forms.

4

Changes in Diclectin Utilization Trends in Ontario Following Media Attention: A Time-Series Analysis

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Introduction: Diclectin (doxylamine and pyridoxine combination) is an antiemetic authorized in Canada to treat nausea and vomiting of pregnancy (NVP), also known as morning sickness. In January 2018, there was extensive media attention following the Toronto Star in Ontario reporting on Diclectin's lack of efficacy according to unpublished clinical trial data submitted for regulatory approval.

Objective: To understand the impact of media coverage on Diclectin utilization in Canada.

Methodology: A time-series analysis of monthly Diclectin dispensing data across Canada from July 2016 to March 2022 was conducted using the IQVIA CompuScript database. Total volume trends of Diclectin dispensed by retail pharmacists in Ontario and across Canada were adjusted for using pregnancy numbers obtained from StatCan birth data. The impact of media coverage in January 2018 on Diclectin utilization was assessed with interventional autoregressive integrated moving average modeling for overall rates and stratified by prescriber specialty.

Results: Diclectin utilization decreased significantly by 1.16% ($p = 0.0150$) in Ontario but did not shift significantly ($p = 0.0642$) across Canada overall. Within Ontario, there was a significant decline of 2.41% ($p = 0.0098$) in Diclectin utilization among family medicine and general practitioners, who also accounted for 391,722 (63.21%) of 619,720 total Diclectin prescriptions. Among obstetrician-gynecologists in Ontario, there was a non-significant decline of 0.50% ($p = 0.2352$) in utilization.

Conclusion: Despite nationwide media attention questioning its efficacy, Diclectin utilization was most impacted only in Ontario, where media coverage was greatest. Our results suggest a lack of alternatives for pregnant individuals suffering from NVP.

5

Prescribing practices of Canadian clinicians for the treatment of moderate-to-severe atopic dermatitis (AD) in the pediatric population (12 years old)

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Background: Pediatric atopic dermatitis (AD) is a chronic inflammatory skin disease that requires special management considerations compared to the adult population. Despite the existence of comprehensive treatment guidelines for pediatric AD, the prescribing preferences and practices of Canadian clinicians in children have not been previously explored. The objective of the study was to elucidate the real-world prescribing practices of Canadian clinicians for the treatment of moderate-to-severe pediatric (<12 years old) AD.

Methods: An expert panel of 5 Canadian clinicians with expertise managing pediatric patients with AD developed a 22-question survey to better understand the prescribing practices of fellow experts caring for pediatric patients with moderate-to-severe AD. The anonymous online survey was emailed to pediatric AD experts across Canada (15/21 completed).

Results: Biologic agents were the preferred option among systemic therapies used to treat this age group as first-line therapy for AD upon failure of topicals (80% of respondents). Among clinical concerns associated with various agent classes, safety concerns were lowest with biologics (13%), followed by phototherapy (40%), prednisone/prednisolone (80%), Janus kinase (JAK) inhibitors (87%). All respondents indicated that pediatric patients are currently being undertreated. Undertreatment was attributed to family hesitancy regarding topical corticosteroids (93%) and inaccessibility of on-label, effective, and safe therapeutic options (93%).

Conclusions: The findings indicate that expert prescribing practice in moderate-to-severe pediatric AD is not aligned with management criteria for older patients due to clinical and safety concerns in patients <12 years. Further consultation is needed to define appropriate criteria in this vulnerable population.

6

Impact of Biosimilar Switching Policy in Ontario: Case-Study of Anti-VEGF Biosimilars

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Background: In March of 2023, Ontario became the latest province to implement pro-active biosimilar switching policies for all patients receiving certain biologic medications. Previously, only funding for new patients had been restricted to biosimilars. Anti-VEGF (aVEGF) therapies account for over $570 million in annual public spend in Ontario. There are currently multiple biosimilar molecules under review or approved by Health Canada for aVEGFs ranibizumab and aflibercept. This analysis estimated possible savings from biosimilar aVEGFs according to different biosimilar switch policies.

Methods: Two scenarios were modelled: a market with complete aVEGF biosimilar switching, and a market with biosimilars used only in new patients. Uptake was based on etanercept and adalimumab biosimilar uptake in Canada. Budget impact over a three-year period was calculated. Costs of other common health care resource utilization were compared to demonstrate the utility of increased savings.

Results: Over a three-year horizon, total Ontario drug plan spend on ranibizumab and aflibercept was estimated to be CAD$997,331,615 following pro-active biosimilar switching, compared to CAD$1,256,861,854 by using biosimilars only in treatment naïve patients. Implementing a pro-active switch policy was therefore associated with an additional CAD$260M in savings over 3 years. These savings are equivalent to the cost of 39,204 average hospital admissions, 853,718 emergency room visits, 143,221 ICU days, or 2.9M physician billings for intravitreal injections.

Conclusions: Adoption of pro-active biosimilar switching policies would dramatically increase drug plan savings, which are essential to bolster the sustainability of the provincial drug plan and can provide efficiencies to the overall healthcare system.

7

Challenges with integrating early endpoints into economic models: Review of CADTH recommendations for adjuvant or neoadjuvant therapies in oncology

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Background: Adjuvant and neoadjuvant therapies for early-stage cancers demonstrate early clinical benefit with endpoints that measure delayed or avoided disease recurrence. Though expected to translate into survival improvement, such benefits take years to confirm. Health technology assessments require economic evaluations projecting lifetime disease trajectories. Thus, assumptions about potential future outcomes are required. We examined economic modelling approaches used in CADTH reviews for adjuvant/adjuvant therapies to understand challenges, explore patterns, and identify opportunities for developing best practices.

Methods: We included CADTH recommendations as of Mar/2023 identified for adjuvant/neoadjuvant treatment of solid tumours with early-stage disease. We collected outcomes and details of submitted clinical and economic evidence. We categorized issues raised in CADTH's economic review, including data maturity, model structure, and long-term benefit assumptions surrounding extrapolation, duration of benefit and cure.

Results: Eighteen submissions were identified for adjuvant/neoadjuvant treatment of solid tumours. Positive recommendations were issued for 78% of reviews, all but one with conditions. OS was noted as immature in all reviews. All 10 reviews with some interim comparative OS data were recommended, while half (4/8) without any OS data were not recommended. Revisions changed implications for cost-effectiveness ($50,000/QALY threshold) in 10/18 reviews. There were inconsistencies in handling treatment-waning assumptions, while cure assessment time was consistently revised to 5 years from initiation.

Conclusions: While all files noted data immaturity, positive recommendations were common. Most economic revisions had modest impact on cost-effectiveness. This research can support further guidance to appropriately capture benefits and assess uncertainties with more consistency in early-stage cancers.

8

Unequal access of innovative dermatology products across Canada

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Background: In Canada, following a pCPA agreement with the manufacturer, the decision to publicly fund drugs belongs to respective public drug plans, which can lead to unequal access across the country. The objective of this analysis was to evaluate the listing status across the public drug plans for the latest innovative dermatology products on the Canadian market.

Methods: Innovative dermatology products that reached a pan-Canadian Pharmaceutical Alliance (pCPA) agreement between January 1, 2016 and June 28, 2023 were collected. The listing status of the products on the public drug plans were recorded. An analysis of percentage listing across drug plans was calculated using all products that had signed a pCPA Letter of Intent (LOI).

Results: There was a total of 11 innovative dermatology products with a signed pCPA agreement. Indications included plaque psoriasis, atopic dermatitis, actinic keratosis, acne, and psoriasis vulgaris. Of the products with a pCPA agreement, the percent listed across the drug plans ranged from 27% to 100%, with the majority listing at least 95%. Ontario, Saskatchewan, Manitoba, New Brunswick, Nova Scotia and NIHB cover 100% of the eleven products. In BC, only 27% (3/11) of the products are listed. The next lowest is PEI at 73% (8/11).

Conclusions: This analysis demonstrates unequal and unequitable access of innovative dermatology products for patients in BC. This situation creates further inequalities for Indigenous communities in BC when compared to the rest of the country as most Indigenous communities in BC do not have access to the NIHB covered medications.

9

Pipeline trends shaping the future of drug development

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Background: The drug development landscape has been evolving over the last few years, from an earlier emphasis on blockbuster drugs developed in-house by large pharmaceutical companies, to niche markets and personalized medicine. This analysis explores key trends shaping the future of drug development.

Methods: This analysis examines new medicines in Phase I, Phase II, Phase III, and pre-registration with clinical trials in Canada, the US, and Europe. GlobalData is the primary data source for this study, in addition to online databases from Health Canada, the US FDA, and the EMA. International markets examined include the US and geographic Europe (excluding Russia and Turkey).

Results: The 2023 drug pipeline contains over 11,500 medicines, compared to just under 10,000 the year before. Oncology continues to dominate the pipeline, representing roughly one third (38%) of medicines in all phases. Over 1,500 new medicines in the pipeline have early orphan designations, one third (33%) of those medicines are in Phase III and pre-registration, which is consistent with the increasing prevalence of orphan-designated medicines entering the pharmaceutical market. Drug development trends in 2023 include the fast-growing biosimilars pipeline, which can provide potential savings and drug coverage sustainability. The gene and cell therapies pipeline has also made substantial strides expanding to new therapeutic areas including novel therapies for Duchenne muscular dystrophy and sickle cell disease.

Conclusion: This research provides a clearer picture of the characteristics and evolution of the pipeline, which will enable policy-makers and other stakeholders to better understand and anticipate emerging drug developments.

10

QT interval prolongation and major adverse cardiac events with donepezil: a scoping review with meta-analysis

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Background: Cholinesterase inhibitors (ChEi) are regularly used in Alzheimer's disease and other dementias. Of the three ChEi, donepezil is the most commonly used and the only one classified as a known risk QT interval-prolonging medication (QTPmed). Given this classification is derived from low-quality observational data, we aimed to evaluate high-quality literature on the frequency and nature of major adverse cardiac events (MACE) associated with donepezil.

Methods: We searched Medline, Embase, International Pharmaceutical Abstracts, and Cochrane Central from 1996 onwards for randomized controlled trials (RCTs) involving patients 18 years or older and comparing donepezil to placebo. The MACE composite included mortality, sudden cardiac death, non-fatal cardiac arrest, Torsades de pointes (TdP), ventricular tachyarrhythmia, seizure and syncope. Random-effects meta-analyses were performed with a treatment-arm continuity correction for single and double zero event studies.

Results: 60 RCTs (n=12,910) were included. Indications for donepezil varied with 24 of 60 trials (n=6,000) investigating participants with Alzheimer's disease. Mortality was the most reported MACE (252/331, 75.8% events), with the remainder being syncope and seizures. There were no reports of TdP, sudden cardiac death, non-fatal cardiac arrests, or ventricular tachyarrhythmias. There was no increased risk of MACE with exposure to donepezil compared to placebo (risk ratio [RR] 1.08, 95% CI 0.88-1.33, I2=0%).

Conclusion: This scoping review with meta-analysis found no evidence that donepezil causes cardiac harm. Further research to clarify actual clinical outcomes related to QTPmeds is important to inform prescribing practices and improve the accuracy of clinical decision support systems.

11

Trends in the use of raloxifene among older adults, 1999 – 2022

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Background: Raloxifene is a selective estrogen receptor modulator approved as second-line therapy for the treatment of postmenopausal osteoporosis. Clinical evidence of raloxifene showed 30-50 % reduction in the incidence of vertebral fracture; however, evidence suggesting higher risk of thrombosis and fatal stroke emerged in early 2000s. Raloxifene was added to the Ontario Drug Benefit (ODB) program in 1999, and the criteria of coverage became tighter in 2003. Health Canada publicized a safety alert highlighting the potential risk of fatal stroke with raloxifene in 2006.

Objective: Describe the number and characteristics of older females initiating raloxifene in Ontario over time.

Methods: We used healthcare administrative databases housed at ICES for this project. Pharmacy claims from ODB were leveraged to identify females utilizing raloxifene based on their first dispensation from 1999/05 to 2022/12. The ODB program covers prescription medications listed on the formulary for residents aged 65 or more years. Therefore, we restricted our inclusion to females 66 years to ensure at least one year of drug plan coverage. The number of incident users (based on the first dispensation) and the number of prevalent users (based on having one or more prescriptions) were plotted by quarter for each calendar year. Additionally, the total cohort was stratified according to the year of initiation into three groups based on key dates that may impact raloxifene drug access: 1999-2002, 2003-2005, and 2006-2022. For every patient category, pharmacy and medical claims in the prior year were utilized to describe patient characteristics (e.g., fracture history, chronic medical conditions, and chronic drug use).

Results: We identified 22,205 eligible females (mean age = 74.2 years, standard deviation = 6.2). The annual number of patients initiating raloxifene peaked at 3879 in 2001 and 3304 in 2002, followed by gradual decline from 2152 in 2003 to 216 in 2014. Only 4% of the total cohort initiated raloxifene between 2015 and 2022. The number of prevalent users was constantly high over the years, yet declined in response to the decreased number of initiations. More than half of patients (55.9%) had a history of oral bisphosphonate exposure while only 5.2% had a history of osteoporosis fracture in the prior year to raloxifene initiation. Hypertension was the most prevailing chronic medical condition in the cohort (61.8%). However, other cardiovascular comorbidities were rare among the total cohort and consistent along the three time periods.

Conclusion: Raloxifene prescribing has declined substantially since 2003, yet persistence on raloxifene continued to be relatively high. Little difference was seen in patient characteristics in the three categories, thus it is hard to estimate the effect of Health Canada safety alert in 2006 outside the drop in the number of initiations. Further research is warranted to understand the safety and benefits of raloxifene therapy in the real-world to inform future prescribing.

12

Cost-effectiveness of palivizumab for the prevention of severe respiratory syncytial virus (RSV) infection in infants born moderate-to-late preterm: Summary of analyses across 4 continents

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Background: Palivizumab is effective for preventing severe respiratory syncytial virus infection (RSV) in otherwise healthy infants born moderate-to-late preterm (32-35 weeks gestational age [wGA]). To support reimbursement decision-making, a new evidence-based cost-utility model (CUA) has been developed that incorporates the International Risk Scoring Tool (IRST). Herein we highlight the application of this model by summarizing analyses undertaken in four different continents: North America (Canada); South America (Colombia); Europe (Italy); and Asia (Korea).

Methods: The analysis included 32-35wGA infants identified as being at moderate- or high-risk of RSVH by the IRST in a decision tree model for palivizumab versus no intervention. Infants were hospitalized with RSV (RSVH), medically attended (emergency room/outpatient) with RSV, or uninfected/non-medically attended and could experience 6-18 years respiratory morbidity across a lifetime horizon. Palivizumab efficacy was drawn from the IMpact-RSV trial (82.2% RSVH reduction). Country-specific parameters for hospital outcomes, costs, and discounting rates were used. The base case used the healthcare provider perspective with no vial sharing.

Results: Palivizumab was found to be cost-effective in all countries: Canada: $18,263/quality-adjusted life year (QALY) vs willingness to pay threshold [WTP] of CAN$50,000 (94.9% probability of being WTP), Colombia: COP$46,810,663/QALY [CAD$14,043] vs WTP of COP$76,396,634/CAD$22,919 (75.4%), Italy: €14,305/QALY [CAD$20,875] vs WTP of €40,000/CAD$58,372 (90.8%), Korea: ₩28,054,307/ QALY [CAD$28,054] vs WTP of ₩45,990,609/CAD$45,991 (75.6%).

Conclusions: Risk factor-guided prophylaxis of 32-35wGA infants is a universal cost-effective strategy versus no prophylaxis. This new CUA has demonstrated utility across different RSV epidemic patterns, geographies and climates, and healthcare systems.

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ASA prophylaxis for preeclampsia prevention: validation within a large administrative dataset

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Background: Clinical guidelines recommend low-dose aspirin (ASA) prophylaxis for women at risk of preeclampsia, a common complication of pregnancy. Since ASA is an over-the-counter medication, capturing real-world ASA prophylaxis is challenging. An Ontario perinatal health registry, the Better Outcome Registry and Network (BORN) database, contains a variable to capture ASA prophylaxis for preeclampsia, but this variable has not been formally validated. Therefore, we aimed to assess the accuracy of the ASA prophylaxis variable in the BORN database against an electronic medical record (EMR) from St. Michael's Hospital (SMH).

Methods: We randomly selected 200 women with prenatal care services or deliveries at SMH from January 2018 to July 2022, irrespective of ASA use. Two independent abstractors extracted ASA use information and maternal sociodemographic characteristics. Accuracy of ASA prophylaxis in BORN was compared to that in the SMH EMR, expressed as sensitivity, specificity, predictive values, and measures of agreement. Additional analyses to account for missing ASA data were performed.

Results: Among 200 women, 24 (12.0%) received ASA prophylaxis for pre-eclampsia (12.5% in the SMH EMR, 8.0% in BORN). Women using ASA prophylaxis were older (37.0 vs 33.0 years) with a history of hypertension (12.5% vs. 5.8%). Sensitivity and specificity of the BORN ASA prophylaxis variable were 62.5% (95% CI 40.6, 81.2) and 100.0% (95% CI 97.3, 100.0), respectively. Specificity remained high throughout additional analyses accounting for missing ASA prophylaxis data.

Conclusions: ASA use within the BORN database is validly collected for potential use in epidemiological studies of ASA prophylaxis for preeclampsia.

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Introduction of subcutaneous administration for existing intravenous treatments; an analysis of reimbursement and regulatory reviews in Canada

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Background: Route of treatment administration can have a large impact on patient quality of care and adherence. Subcutaneous (SC) administration may provide advantageous convenience, patient quality of life, and healthcare resource utilization profiles compared to intravenous (IV) administration. The objective of this analysis was to examine the introduction of SC use for existing IV treatments in the Canadian treatment landscape by capturing regulatory and reimbursement histories over the last 15 years.

Methods: Reimbursement and regulatory review histories were collected from the Health Canada (HC) Drug Product Database (DPD), HC Notice of Compliance (NOC) Search, and publicly available reviews, recommendations and negotiation summaries from Canadian Health Technology Assessments (HTA), and the pan-Canadian Pharmaceutical Alliance (pCPA). Outcomes examined included timing for introduction of SC treatments to their public funding in Canada.

Results: Ten SC treatments received NOC following IV (4 in oncology, 5 in non-oncology, 1 in both). Average time from first IV NOC to SC NOC was 9.6 years (range, 4-20 years). Average time from SC NOC to pCPA conclusion was 17.1 months. In general, time required for regulatory review and public funding was similar between oncology and non-oncology medicines. Ultimately, fewer oncology treatments achieved public funding (50%) than those in non-oncology (67%).

Conclusions: Given issues with healthcare human resources, SC administration of existing IV treatments is important to consider to reduce treatment administration burden. In Canada, introduction of SC use for existing IV treatments can be slow and their adoption for public funding has been mixed.

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Using administrative data to guide health service and health human resource planning for COPD: incidence, prevalence, and utilization of health services among patients in Ontario Canada from 2005-2015.

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Background: Chronic Obstructive Pulmonary Disease (COPD) is a chronic condition that is categorized as an ambulatory care sensitive condition, meaning access to quality care can reduce complications and health care usage. This study outlines the incidence, prevalence, and the utilization of health services - such as physician visits, emergency department (ED) visits, and hospital admissions among the residents of Ontario, Canada, as a means to investigate access to primary care services.

Methods: In this retrospective longitudinal cohort study, we used administrative data from Ontario, Canada's ICES dataset. COPD patients were ascertained through a validated algorithm from 2005 to 2015. We computed age and sex-standardized rates of incidence, prevalence, and health service use (physician visits, ED visits, hospitalizations) overall. The standard population was from the 2015 statistics Canada census.

Results: Results are reported for females and males aged 60-69 in 2005 and 2015 per 100,000 population in the standard population. The crude incidence of COPD was 591, and 710, for males 700, and 923. The crude prevalence was 8,859 and 16,013 for females and 9,765, 18,010 for males. The crude incidence of all cause ED visits among females was 955, 126, and 1,081, and 174 among males. All cause hospitalization was 641, 769 for females and 700, 923 for males. The crude occurrence of physician visits was 10,860, 1,622 and for males 11,036, 1,937.

Conclusion: COPD is a chronic illness that exerts a large burden on Ontario’s health care system. Stratifying by geographic groups to measure health services utilization and delivery in these populations could target underserved populations like rural or remote areas, supporting decision making related to policy and health human resource planning.

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Coordination of oral anticoagulant care at hospital discharge (COACHeD): pilot randomised controlled trial

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Background: Oral anticoagulants (OACs) are high risk medications and adverse event rates are especially high after hospital discharge.

Methods: A randomized parallel trial enrolling adult patients about to be discharged from medical wards at 6 Ontario hospital sites taking an OAC. The interdisciplinary intervention was led by a clinical pharmacologist and included a detailed discharge medication reconciliation and management plan focused on OACs; a circle of care handover; and early post-discharge virtual check-up visits to 1 month with 3-month follow-up. The control group received usual care.

Results: Extensive periods of restriction of recruitment plus difficulties accessing patients at discharge negatively impacted feasibility. Of 845 patients screened, 167 were eligible, 56 were recruited (mean age 71.2 SD 12.5 yr, 42.9% female) with 2 lost to follow-up. 47 (84.1%) were discharged on a DOAC, 18 (32.1%) were new users. Intervention patients were significantly more likely to recall OAC education than control (X^2 5.89, p=.015), to rate their continuity of care higher (X^2 24.5, p < .00001), their ability to manage their OAC as improved (X^2 4.70, p =.03), to report less medication bother (X^2 10.1, p=.0015) and to end up on fewer inappropriate medications (X^2 14.5, p = 0.001). There were no significant differences for OAC knowledge, quality of life, health care utilization or adverse anticoagulant safety events.

Conclusion: This pilot trial suggests that a transitional OAC management intervention at hospital discharge was well received, but overly difficult to administer. Future studies should expand the scope to include other high risk medications.

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International generic availability improvements between 2010 and 2021

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Background: Drug shortages can in many cases be mitigated by a competitive generic market, which provides multiple offerings of products that can be used interchangeably for those in shortage. This research aims to provide an overview of Canada's generic drug market's vitality in comparison with that of its international peers.

Methods: The study uses oral solid drug sales data from IQVIA's MIDAS database and population data from the OECD for the period 2010-2021. We investigate trends in the number of companies selling generics, the distribution of medicines sold by a number of available generics, generic sales as a proportion of total pharmaceutical sales, and sales per capita. We compare Canada's generic market to that of the eleven comparator countries used by Canada's Patented Medicine Prices Review Board (the PMPRB11) and of the United States.

Results: Despite Canada counting relatively few generic companies, its generic availability and sales of generics ranked high relative to countries with a similar pharmaceutical landscape. The proportion of oral solids sold in Canada for which generics were available was 84% in 2021, above the PMPRB11 median of 72%. Canada's generic spending per capita was $137 in 2021, well above PMPRB11 countries, which spent a median of 64$ per capita, and the United States, which spent $108 per capita.

Conclusion: International generic availability and competition indicators overall considerably improved since 2010.

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Evaluating the Lorlatinib Patient Support Program Real-World Evidence (RWE) project in the context of CADTH's guidance for reporting RWE: what constitutes robust RWE?

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Background: Lorlatinib is the only targeted therapy indicated for advanced anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC) that has progressed on prior next-generation ALK inhibitors. In January 2020, due to uncertainty of Phase II data, lorlatinib received negative HTA recommendations for this rare indication with high unmet need. In August 2020, a prospective Canadian real-world evidence (RWE) generation project leveraging the Lorlatinib Patient Support Program (PSP) infrastructure was initiated to describe lorlatinib effectiveness and quality of life.

In the context of CADTH's recent Guidance for RWE Reporting document, the objective was to evaluate alignment between the Lorlatinib PSP RWE project (i.e., design, methodology, analysis, and reporting) and CADTH's RWE Guidance.

Methods: The industry-based project team evaluated all existing and approved project documentation to CADTH's final RWE Guidance checklist.

Results: Of the 96 checklist items, 77.1% (n=74) were applicable to this RWE project. Among applicable checklist items, 90.5% (n=67) of the items were complete and the other 9.5% (n=7) could be completed (e.g., describe governance structure) based on existing documentation. For completed items, 58.2% (n=39) were completed prior to analysis (i.e., protocol, ethics, data management plan, statistical analysis plan, data dictionary) which is key to robust and transparent execution; the other 41.8% (n=28) were completed after analysis (i.e., analysis outputs, conference abstracts/posters, manuscript).

Conclusions: We evaluated the Lorlatinib PSP RWE project against CADTH's RWE Guidance. Despite not having a reference checklist at the time of RWE conception, our analysis suggests robust RWE design and reporting which facilitates RWE evaluation.

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A survey of the current glaucoma treatment landscape in Canada

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Background: Open-angle glaucoma (OAG) is a leading cause of blindness in North America. The utilization of selective laser trabeculoplasty (SLT) in Canada is unclear and requires investigation.

Methods: Canadian eye care specialists participated in an online survey between May 18th - July 21st, 2022. They were screened to ensure they were in practice for more than two years; have at least 30 mild-to-moderate glaucoma patients; treat at least one new case of mild-to-moderate glaucoma per month. Descriptive analyses are reported.

Results: In total, 70 ophthalmologists participated across Canada and were asked to self-report their typical treatment for a naive mild-to-moderate glaucoma patient. First-line treatment: 66% of ophthalmologists start with eye drop monotherapy, 24% SLT only, 9% on 2+ classes of drops (one or more bottles), 1% SLT plus drops. If the patient did not reach sufficient IOP reduction, in Step 2 = 39% of ophthalmologists add another class of drops, 33% switch to a new monotherapy class of drops, 17% SLT + drops, 9% SLT only, 3% other. If patients still do not reach sufficient IOP reduction, a Step 3 was captured. In addition, ophthalmologists reported that in a typical year, 32% of patients treated with SLT only do not achieve sufficient IOP reduction and need to be switched to another treatment. Typically, within a year, over half (59%) of ophthalmologists add drops after a first SLT is performed.

Conclusions: While most OAG patients are still being treated with eye drops in first and subsequent lines, SLT (with or without drops) has become a common intervention. Over half of ophthalmologists reported need for drops after SLT.

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Real-World third-line treatment pattern in Canadian HER2+ Metastatic Breast Cancer Patients

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Exactis Innovation

Background: HER2-positive (HER2+) breast tumors constitute 15-30% of newly diagnosed breast cancer (BC) cases, impacting approximately 27,640 patients in Canada. Within this group, 6-10% receive a metastatic stage (mBC) diagnosis. Targeted therapies have significantly improved outcomes. In 2018, the standard first-line treatment involved trastuzumab, pertuzumab, and taxanes, followed by trastuzumab emtansine (T-DM1) as the second-line approach. However, consensus on optimal third-line therapy remained elusive despite the approval of treatments like tucatinib, neratinib, or lapatinib.

Methods: This study aimed to assess recent clinical practice evolution and identify gaps in post-second-line therapy for this patient population. Retrospective data from medical records of 66 patients who received third-line treatment before October 31st, 2018, and data from 56 patients who received third-line treatment after this date, extracted from the Personalize My Treatment (PMT) cancer patient registry, were analyzed.

Results: In the initial cohort, the study unveiled diversity in third-line therapeutic strategies, with trastuzumab, lapatinib, and T-DM1 as primary choices. Data were collected before the widespread availability of tucatinib, neratinib, and trastuzumab deruxtecan in Canada. Nevertheless, the PMT cohort exhibited the emergence of novel therapeutic combinations, including trastuzumab combined with pertuzumab or tucatinib, often administered alongside capecitabine. Additionally, a shift from lapatinib to a preference for T-DM1 was observed.

Conclusion: These findings underline the evolving landscape of third-line treatment in Canada, emphasizing the need for additional therapeutic options. This study provides valuable insights into the current state of third-line treatment in Canada and underscores the importance of expanding treatment choices to enhance patient outcomes.

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Comparative effectiveness of biosimilar drugs versus their equivalent legacy drugs: The CAN-AIM Biosimilar Registry

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Background: Concerns remain about the safety and effectiveness of biosimilars versus their originator. We present preliminary findings on discontinuation and clinical remission for biosimilar versus reference drugs in rheumatoid arthritis (RA) and inflammatory bowel disease (IBD) in the real world.

Methods: This is a proof-of-concept pan-Canadian clinical registry of adults (≥18 years) with RA/IBD initiating biosimilar or equivalent legacy drugs (2015-2023). We compared discontinuation of infliximab biosimilar (INF-B) versus bio-originator (INF-O) in IBD and etanercept biosimilar (ETA-B) versus bio-originator (ETA-O) in RA. For ETA, we also compared RA control (Disease Activity Score 28 ≤2.6, Simplified Disease Activity Index ≤3.3, or Clinical Disease Activity Index ≤2.8). We produced adjusted hazard ratios (aHR), controlling for age, sex, calendar year, past biologics, and disease duration for all analyses, plus disease activity for ETA analysis and underlying indication, race/ethnicity, smoking, and corticosteroids for the INF analyses.

Results: IBD initiators (n=445) of INF-B or INF-O had similar discontinuation rates: aHR for INF-B versus INF-O was 0.77 (95%CI 0.47-1.26). RA initiators (N=250) of ETA-B and ETA-O had similar discontinuation rates at 12 months (ETA-B versus ETA-O aHR 0.82, 95%CI 0.42-1.60) but slightly lower at 24 months (aHR 0.51, 95%CI 0.26-0.98). In those not initially in RA remission at ETA initiation (N=150), time to first remission was not different for ETA-B versus ETA-O (aHR 1.43, 95%CI 0.65-3.13).

Conclusions: In this Canadian real-world cohort of RA and IBD patients, we did not find higher discontinuation/remission with INF/ETA-B Future evaluations include quality of life and safety (e.g., infection).

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Cost-effectiveness of olaparib vs. rucaparib for patients with metastatic castration-resistant prostate cancer – The Canadian perspective

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Introduction: Through phase III clinical trials, olaparib (ola) and rucaparib (ruca), (poly(adenosine diphosphate ribose) polymerase inhibitors) have demonstrated outcome improvements in metastatic castration-resistant prostate cancer (mCRPC) patients with alterations of BRCA1/2 and having progressed on second-generation androgen-receptor pathway inhibitor (ARPI). While improving outcomes, ruca and ola contribute to the ever-growing economic burden of PCa. Cost-effectiveness analyses are needed to estimate their economic impact.

Objectives: To evaluate the cost-effectiveness of ola and ruca versus physician's choice (docetaxel or ARPI) for mCRPC patients with BRCA1/2 mutations in a Canadian healthcare setting.

Methods: Partitioned survival models were created to represent mCRPC disease after progression on ARPI until death or 5 years. Survival inputs were extracted from PROfound and TRITON3. Ola costs were extracted from the Quebec Health Insurance Board medication list. As ruca is not commercially available in Canada, we hypothesized that it will be priced on par with ola.

Results: Our findings suggest that ruca provides better survival benefit in terms of quality-adjusted life years (QALY) than ola, but at a higher cost (ICER $302,158/QALY). When compared to docetaxel, ola and ruca provided additional 0.27 and 0.44 QALY with additional costs of $81,756 and $131,193, resulting in ICERs of $299,022/QALY and $300,196/QALY respectively. When compared to ARPI, ola and ruca demonstrated clinical benefit and ICERs of $565,057/QALY and $416,204/QALY respectively.

Conclusions: While providing survival benefit to mCRPC patients presenting alterations of BRCA genes, the cost of ola and ruca requires major reductions to be considered cost-effective in the Canadian healthcare perspective.

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Trends in opioid-related toxicities among people with and without opioid use disorder in Ontario

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Background: The drug toxicity crisis has continued to accelerate across Canada, driven by an unpredictable unregulated drug supply. We sought to characterize trends in opioid toxicities, among people with and without opioid use disorder (OUD) and assess the impact of the COVID-19 pandemic.

Methods: We conducted a population-based study of all individuals in Ontario who experienced a fatal or non-fatal opioid toxicity between January 1, 2014, and December 31, 2021, using administrative healthcare data housed at ICES. We used interventional autoregressive integrated moving average (ARIMA) models to evaluate the impact of COVID-19 on event rates. All analyses were stratified by people with and without OUD.

Results: Overall, we identified 80,296 opioid toxicities, with an over four-fold increase observed between January 2014 (N=356; 2.6 per 100,000) and December 2021 (N=1,571; 10.5 per 100,000). Among these individuals (mean age: 40.5 years; 64.0% male), 14% (N=11,164) experienced fatal opioid toxicities and approximately 50% had OUD. We observed a significant ramp increase in the rate of opioid toxicities following the onset of COVID-19 in March 2020 [0.2 per 100,000 (~30/month), p=0.02]. We found a similar ramp increase among people with OUD (0.2 per 100,000, p <.001), however this was not significant among people without OUD (p=0.95).

Conclusion: The rate of opioid toxicities has continued to grow across Ontario, with substantial acceleration during COVID-19. The important differences observed among people with OUD compared to those without, highlights the critical need for improved access to harm reduction programs and the continued monitoring of opioid-related harms post-pandemic.

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Reimbursement Outcome Analysis for New Oncology Products in Canada

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Background: New oncology drug submissions to the Canadian Agency for Drugs and Technologies in Health (CADTH) are crucial in enhancing oncology drug access for Canadians by ensuring academic evaluation and potential approval of innovative treatments. Phase II trials can offer valuable information on the clinical effects of drugs, and their inclusion in the review process offers valuable clinical insight. The objective of this analysis was to summarize oncology products that have received a positive CADTH recommendation using Phase II studies with overall response rate (ORR) as a primary or secondary endpoint.

Methods: A review of publicly available reimbursement recommendation reports from the CADTH website between January 2020 to September 2022 was conducted. Each submission was evaluated on their phase of clinical trials, ORR data, the drugs' ability to fulfill unmet needs, and their final recommendation.

Results: A total of 94 completed CADTH oncology drug reviews were assessed. Of the reviews that provided Phase II or III trials as clinical evidence (n=91), 23% (21/91) submitted Phase II clinical trials as pivotal trials. 62% (13/21) of Phase II trials received a positive reimbursement recommendation. 75% of reviews with phase II and ORR data that were positively recommended fulfilled the unmet need for limited treatment options. All negative recommendations were associated with no significant improvement in ORR (9/63).

Conclusions: Through the analysis of drug submissions, reimbursement recommendations, therapeutic profiles, and unmet needs, this assessment contributes to a deeper understanding of CADTH oncology reviews and the importance of key outcomes in making funding recommendations.

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Leveraging real-world data from the private payer prior authorization process to operationalize an outcomes-based agreement in Canada

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Background: Timely access to novel therapies has become increasingly challenging due to the rising number of therapies with limited but promising evidence, coupled with long reimbursement timelines. Outcomes-based agreements (OBAs) are a potential solution to enable early access for patients to therapies, while mitigating the risk for payers of non-performance in the real world. One key barrier to the adoption of OBAs in Canada is the availability of appropriate real-world data (RWD) to support such agreements. This study sought to evaluate if existing prior authorization (PA) processes used by private payers could be leveraged to support OBAs.

Methods: A selection of publicly-available PA forms were reviewed to identify health outcomes currently being collected. Qualitative interviews were then conducted with private insurers and PBMs in Canada from May to October 2022, via Microsoft Teams. 14 organizations were invited to participate; 8 organizations participated, with 15 individuals in attendance. 20 interview questions were discussed across 4 themes: prior authorization (PA), OBAs, OBAs and PA, and OBA financial models.

Results: More than 20 health outcomes are currently collected in private payer prior authorization forms. However, the private payer PA process is currently not usable to generate RWD to support OBAs.

Conclusions: Incentives for leveraging the PA process for RWD generation to support OBAs are currently limited in the private payer space. It is anticipated that stakeholders will continue to investigate PA infrastructure use to support RWD for OBAs, with rare disease drugs potentially being a catalyst.

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Forecasting the Coverage of Patients with Alzheimer's Disease by Public and Private Insurers in Different Canadian Jurisdictions

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Background: Alzheimer's disease (AD), a progressive neurodegenerative condition, gradually impairs cognitive function and memory. As the Canadian population ages, AD poses an increasing burden on the healthcare system. Since the onset of AD coincides with the transition from private to public coverage for many Canadians, it is a challenging task to accurately predict resource burden for patients with AD in the Canadian public and private payer markets.

This study utilized the Canadian Health and Reimbursement Insurance Simulation (CHRIS) model, developed by PDCI Market Access/McKesson (Canada), to estimate the number of diagnosed lives of AD patients across different Canadian jurisdictions. Additionally, the study estimated the public-private split in healthcare coverage for this patient population and the implications for manufacturers and private insurers during the extended period of HTA evaluation prior to potential public formulary listings.

Methods: Data on the Canadian prevalence of AD were obtained from published literature. Population distribution across Canadian jurisdictions was obtained from Statistics Canada. The potential distribution of public and private reimbursement eligibility was estimated using internal research conducted by PDCI/McKesson (Canada).

Results and Conclusion: We simulated the payer mix of AD patients and their respective public and private eligibility across Canada. The age distribution and reimbursement eligibility of potential AD patients resulted in complex reimbursement considerations during the early phases of product introduction for new AD medicines anticipated in Canada in the next few years. Overall, the findings of this study lay the groundwork for future comprehensive cost predictions of public and private coverage in Canada.

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The Impact of Patient Proximity to Clinic on Patient Persistence and Compliance in Canada

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Innomar Strategies

Patient appointment data in conjunction with longitudinal pharmacy dispensing data were used to better understand the relationship between how far a patient travels and their persistence and compliance on infused medications.

Persistence and Compliance have long been shown to be inversely impacted by out-of-pocket patient costs, while the impact of distance to physician or distance to dispensing pharmacy has not been found to consistently influence these levels. Given the growth in the use of high-cost specialty and rare disease medications requiring specific handling and cold chain distribution to specialized clinics, the role of clinic proximity on persistence and compliance was examined.

Clinic appointment data for the past two years were analyzed to identify patients on an infused medication who consistently used only one clinic over time. Distances between the patients and the clinics they used were calculated based on the distance between Forward Sortation Areas (FSAs). Patients were sorted into three groups based on distance travelled (40km, 40-80km, and over 80km). Dispensing data was then used to evaluate persistence and compliance for each group.

Persistence was not found to differ significantly across groups, however compliance did drop as the distance to their clinic increased. This suggests that while patients tend to stay on their medications regardless of proximity to their clinic, they are more likely to skip, miss, or stretch out the time between patient visits as the distance grows. This insight is relevant as improved persistence and compliance, are generally accepted to improve health outcomes.

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Determinants of non-adherence to HAART among displaced PLHIV and comparison of adherence between displaced PLHIV and hosts: An analytical cross-sectional study in Ituri and North Kivu

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Introduction: Little information is available on the extent of HIV and adherence to Highly Active Anti-retroviral Therapy (HAART) among displaced people living with HIV (PLHIV). The objective of this study was to compare the prevalence of non-adherence between displaced PLHIV and hosts, and to identify the determinants of non-adherence among displaced PLHIV in order to formulate innovative recommendations to facilitate treatment adherence.

Methods: A cross-sectional analytical study including 444 adult PLHIV, displaced and hosts was conducted in Ituri and North Kivu from November 2022 to January 2023. Adherence was assessed by patient self-reporting and prescription refills over the past three months. U-Mann Withney and Chi-2 tests were performed. Logistic regression in SPSS 22 was used to identify the determinants of non-adherence.

Results: The prevalence of overall noncompliance was higher among displaced PLHIV compared to those in the host population: 30% (24.2%-30%) vs. 21% (18%-24%).The prevalence of non-adherence among displaced PLHIV was not different between the two provinces: 25.6% (18%-34%) in Ituri vs 34% (25.8%- 43.2%) in North-Kivu. Displaced PLHIV had a longer diagnosis-to-treatment duration (2 months vs 0 months, p=0.000). The main reasons for not taking antiretroviral therapy among displaced PLHIV were: forgetfulness, lack of food, occupation and travel. Multivariate analysis identified camp-to-hospital time greater than one hour (ORa:2.3;95% CI:1.21 - 7.20), patient dissatisfaction (ORa:6.2;95% CI:2.16 - 17.7), opportunistic infections (ORa:5.3;95% CI:1.8 - 15.5), and stigma (ORa:7.3;95% CI:2.8 - 18.8) as determinants of non-adherence.

Conclusion: Forced displacement favors non-adherence to HAART. The specificities of displaced PLHIV require specific strategies to improve their retention on HAART in order to reduce HIV-related morbidity and mortality.

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Efficacy and safety of cannabinoids in treating spasticity and other symptoms of multiple sclerosis: a double-blind, randomized, placebo-controlled trial protocol

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Background: Multiple sclerosis (MS) is a chronic neurological autoimmune disease that affects 90,000 Canadians. A previous Canadian survey revealed that 65% of people with MS (PwMS) have used medical cannabis to relieve MS symptoms, despite the lack of robust evidence regarding its efficacy and safety. Therefore, we will assess the efficacy and safety of tetrahydrocannabinol (THC), cannabidiol (CBD), or their combination in relieving spasticity and other key MS symptoms.

Methods: In this double-blind factorial trial, we will recruit 250 PwMS over 21 years, from the University of Montreal Health Centre, with a self-reported spasticity of 2 in the numeric rating scale (NRS). Participants will be randomly assigned to receive THC only, CBD only, THC + CBD, or placebo, and followed for four weeks. The primary outcome is the change from baseline in the mean NRS. Secondary outcomes include the clinical investigation of spasticity, mobility, cognition, and safety, in addition to self-reported pain, sleep, bladder, bowel, and sexual dysfunctions, the restless legs syndrome, mental health, and quality of life. Markers of MS will also be assessed. Treatment responders who will improve their spasticity by 1 in the NRS will be eligible for an extension follow-up of 12 weeks.

Results: As of June 16, 2023, 108 participants were approached, from whom 36 have been enrolled. Of these, 28 were randomized. Recruitment and data collection is currently in progress and is expected to end in 2025.

Conclusion: Findings will provide insights in establishing clinical practice guidelines regarding the symptomatic treatment of MS with cannabinoids.

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CORTEX: Partnering neurotech companies and community organizations for real-world validation and brain health impact

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Background: The Ontario Brain Institute (OBI) is a provincially funded non-profit committed to improving brain health by advancing evidence-based brain health solutions. We develop and deliver programs that fill gaps to move innovations from lab to life. The current work describes the process and key outcomes from a new program that partners community groups and companies to conduct real-world validation and scale of brain-related technologies.

Methods: The OBI supported a landscape analysis to identify successful pathways for innovation adoption. We then conducted stakeholder consultations with community organizations, neurotech companies and multinational enterprises to develop the framework for the program. We piloted the CORTEX (Community-based real-world neurotech experience) program with 8 projects, with each project building from our lessons learned.

Results: The landscape analysis identified the important role of patient advocacy groups and community organizations in assisting with the adoption of technology. The stakeholder consultations showed a 98% buy-in for the concept of CORTEX. Through 8 pilot projects, we have seen over 1100 individuals get access to technologies that support their brain health; 1 product secure reimbursement status through a government program; and built capacity in the community for conducting real-word studies

Discussion: Through co-creation and partnership, CORTEX has developed into a program that can assist with real-world validation of neurotechnology and build capacity in the community to conduct real-world studies. The early success of CORTEX has allowed us to reimagine the potential for conducting validation and post-market surveillance in partnership with community organizations, to improve the brain health of Canadians.

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The Canadian Cancer Real-world Evidence Platform: Generating actionable RWE to answer decision-maker questions

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The number of novel oncology pharmaceuticals is rapidly increasing, with cancer therapeutics occupying a substantial portion (25%) of public drug spending in Canada. However, there remains a knowledge gap between drug efficacy and effectiveness, as clinical trials are conducted with potentially small sample sizes, strict eligibility criteria, single-arm design, lack of relevant Canadian comparators, and short follow-up periods for study outcomes. There is thus a growing need for post-market drug evaluations (PMDE) using real-world evidence (RWE) to ensure that cancer therapies are safe, effective, and clinically relevant.

Launched in September 2022, the Canadian Cancer Real-world Evaluation (CCRE) Platform is a pan-Canadian network that supports CADTH's CoLab in PMDE. The CCRE consists of a diverse group of individuals with advanced expertise in pharmacoepidemiology, health services research, health technology assessment, biostatistics, cancer-related health policy, and patient engagement. The team is embedded in provincial cancer agencies in Ontario, Alberta, and British Columbia, with in-house access to health administrative data. This includes population-based data on systemic treatments, radiation, and surgery, in addition to other health services utilization data. In the remaining provinces, data may be obtained through CCRE's collaborations with the Health Data Research Network Canada and the CanREValue Collaboration. Databases available to the CCRE are updated in a timely manner, with some having only a 2-month lag from real-time data collection.

Leveraging pan-Canadian data, we have developed a flexible three-stream response system to triage queries based on the complexity and resources required to generate timely oncology RWE for decision-makers in Canada.

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Beyond health technology assessment recommendation: a comprehensive review of interprovincial variations in cancer drugs funding in Canada

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Background: The funding process for cancer drugs in Canada is complex, with multi-step regulations. Despite implementing the pan-Canadian Oncology Drug Review (p-CORD), interprovincial variation in funding decisions still exists across Canada because each province makes decisions. Until now, little is known about the provincial funding process and its impact on cancer patients.

Methods: We conducted a comprehensive review of studies through electronic databases and governmental websites. We aimed to identify (a) factors considered in the provincial funding process for cancer drugs, (b) outcomes resulting from interprovincial variation, and (c) solutions to guide policy and practice about provincial funding for these drugs.

Results: A total of 17 studies published from 01/2012 to 04/2022 and 34 reimbursement reports from Canadian Agency for Drugs and Technologies website from 2017 to 2019 met the inclusion criteria. Every province considered various factors in their funding decisions, including p-CODR recommendation, clinical benefits, cost-effectiveness, provincial capacities, stakeholder preferences, cancer type, and other factors. Interprovincial variation in funding decisions resulted in consequences: delay in access to treatment, negative health-related quality of life, and patients' and physicians' choices of treatment. Some solutions that could facilitate the provincial funding process included using real-world evidence, stakeholder collaboration, and trade-off considerations.

Conclusion: This review outlined different factors considered in the funding process, which might result in interprovincial variations in funding decisions. These decisions impacted patients and cancer systems. Future research including intervention points is required to reduce variation in funding processes and ensure fair access for cancer patients and reduce healthcare costs.

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An Innovative Approach to Generate Patient-Centered Evidence in a Real-World Evidence Setting

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Canadian payers and policy makers recognize the value of real-world evidence (RWE) and patient-reported outcomes (PROs) to better inform funding decisions. However, only few organized structures allow to collect this type of data in Canada. The PROxy Network is an innovative research web-based platform designed to facilitate the generation of patient-centered evidence. Participant recruitment and identification is ensured by an established network of community pharmacies, patients' associations, or healthcare professionals. PROs collected through a PROxy study include signs and symptoms, activities impairment, work productivity loss, quality of life and preference-based measures, health care resource utilization, treatment satisfaction, and caregiver burden. This network allows conducting longitudinal or cross-sectional RWE studies. All PROxy Network studies are reviewed and approved by an independent ethics committee and meet the highest standard for confidentiality and security of data. RWE generated by the PROxy Network enriches the value proposition beyond traditional safety and clinical efficacy to optimize the market access of innovations. The PROxy Network generates RWE in a timely manner and fills a gap in collecting Canadian patient-centered evidence. In conclusion, data collected through the PROxy Network will allow to place the patient's voice at the core of health decisions. As an example, a PROxy study demonstrated that, despite current acute treatments, the burden of migraine on productivity is high in Canada, with an average percentage of productivity loss due to presenteeism (12.1%) two-times higher than absenteeism (6.9%) and an average cost of $772.74 per patient per months.

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Enabling improvement in CAR T-cell therapies in Canada

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During a one year project, CPHIN and its partners used an action research approach to understand opportunities to improve quality of CAR T-cell therapy in Canada and to improve collection and use of data describing CAR T-cell therapy. This initiative engaged clinicians, scientists and leaders involved in CAR T-cell therapy from across Canada, including the execution of semi-structured, qualitative interviews with hematologists at the major CAR T-cell treatment and referring centres, including: BC Cancer Agency, Tom Baker Cancer, Saskatchewan Cancer Centre, Princess Margaret Cancer Centre, Kingston Health Sciences Centre, The Ottawa Hospital, McGill University Health Centre, CHU de Quebec, and Nova Scotia Cancer Centre. These discussions were supported by analysis of the data submitted to the Center for International Blood and Marrow Transplant Research.

As a part of this initiative, CPHIN successfully engaged and collaborated with a diverse group of industry stakeholders to identify process improvement opportunities, and is now working to implement recommended solutions. From this methodology, the following key ecosystem collaboration learnings were identified: Frequent and transparent communications are needed to maintain momentum, inform next steps, and build a network of trust and security. Action is pushed through the coalition of the willing, to build credibility and later achieve broader acceptance. Stakeholder participation is garnered by first building a foundation of trust.

CPHIN is now advancing this collaborative effort and learnings, leveraging ecosystem partnerships to implement the identified solutions of a referral network and Canadian data registry.

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The MOSAIC Study: A clinical and humanistic burden of illness study among patients with geographic atrophy (GA) and their caregivers in the United States (US) and Canada (CA)

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Background: GA is a progressive advanced form of age-related macular degeneration with incidence and burden rising globally. MOSAIC characterized the burden of illness in GA patients and their caregivers in the US and CA.

Methods: A survey with 149 patients (102 US, 47 CA) and 148 caregivers (102 US, 46 CA) was conducted.

Results: There were more male patients and male caregivers in CA (62% and 61%, respectively) than in the US (43% and 47%, respectively). Mean patient age was lower in the US than in CA (68 vs 73 years, respectively); mean caregiver age was similar in both countries (46 US, 44 CA). Visual changes due to GA were reported in both eyes by 43% of US and 47% of CA patients. Most patients received help from children (41% US, 34% CA) or partners (39% US, 47% CA). Mean National Eye Institute Visual Function Questionnaire-39 composite scores were comparable in both countries (44.6 US, 48.3 CA). More US patients reported needing daily help (68%) than CA patients (38%). A majority of patients (95% US, 97% CA) gave up driving due to their eyesight. Caregivers mostly cared for their partner in the US (37%) vs their parent (65%) in CA. Most (63%) CA caregivers had moderate to severe burden (per Zarit Burden Interview) vs 15% of US caregivers. US dyad data (n=93) showed moderate correlation (r=-0.63) between the burden of patients and caregivers.

Conclusions: In the US and CA, GA burden on patients and their caregivers is substantial.

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