TITLE:
Medication Use and Its Impact on Older Adult High Cost Healthcare Users: Protocol for the Population-Based Matched Cohort HiCOSTT Study

AUTHORS:
Justin Lee, MD, BScPhm[1,2]
Sergei Muratov, MD, PhD[2]
Jean-Eric Tarride, PhD[2,3]
J. Michael Paterson, MSc[4,5]
Kednapa Thavorn, PhD[5,6]
Lawrence Mbuagbaw, MD, PhD[2]
Tara Gomes, PhD[4,7]
Wayne Khuu, MPH[4]
Hsien Seow, PhD[2,8]
Lehana Thabane, PhD[2]
Anne Holbrook, MD, PharmD[2,9]

[1]Division of Geriatric Medicine, Department of Medicine, McMaster University, Hamilton, Ontario, Canada
[2]Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada
[3]Center for Health Economics and Policy Analysis (CHEPA), McMaster University, Hamilton, Ontario, Canada
[4]ICES, Toronto, Ontario, Canada
[5]Institute of Health Policy, Management, and Evaluation, University of Toronto, Toronto, Ontario, Canada
[6]Ottawa Hospital Research Institute, The Ottawa Hospital, Ottawa, Ontario, Canada
[7]Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Ontario, Canada
[8]Department of Oncology, Faculty of Health Sciences, McMaster University
[9]Division of Clinical Pharmacology and Toxicology, Department of Medicine, McMaster University, Hamilton, Ontario, Canada

CORRESPONDING AUTHOR:
Justin Lee
Geriatric Education and Research in Aging Sciences (GERAS) Centre
88 Maplewood Avenue, Room 158
Hamilton, Ontario, Canada, L8M 1W9
Email: justin.lee@medportal.ca

WORD COUNT: 2545 (excluding title page, abstract, references, tables and figures)

ABSTRACT

Background:

High cost users (HCUs) are a small proportion of the population that use disproportionate healthcare resources. A better understanding of their multi-morbidity and drug use is needed to inform health interventions and policies. The main objectives of this study are to determine the clinical and financial contributions of prescription medications to healthcare system expenditures and the development of incident HCU status in older adults.

Methods:

Retrospective population-based matched cohort analysis of newly incident older adult HCUs defined as Ontarians aged 66 years or older in the top 5% of healthcare expenditure users in fiscal year 2013, but not in the prior fiscal year. Person-level data (e.g. demographic, drug and healthcare utilization) for the index year and year prior to HCU status will be obtained from linked health administrative databases. Each HCU will be matched to three non-HCUs based on age, sex and geographic location. Medication utilization will be cross-referenced to chronic conditions and reasons for hospitalization to identify whether suboptimal prescribing may be contributing to adverse outcomes. Regression analyses will be conducted to explore the relationship between the use of specific medication classes and incident high cost healthcare status.

Interpretation:

With its matched study design and focus on incident rather than prevalent high cost healthcare users, this study's results will determine whether prescription medications and the quality of their

prescribing are important triggers of HCU status and facilitate the identification of potential preventative clinical interventions

Trial Registration Number:

Registered with clinicaltrials.gov (registration number: NCT02815930)

Word Count: 245

BACKGROUND

High cost healthcare users (HCUs) are a small segment of the population that use disproportionate healthcare resources. In 2011, 5% of individuals in Ontario, Canada accounted for 65% ($19.8 billion) of the province's total measured healthcare expenditures.(1) With costs expected to double in 20 years, the current approach to HCUs has been deemed unsustainable.(2) Similar findings have been reported internationally including the United States, United Kingdom and Australia.(3–5) Despite increasing international scrutiny, the clinical epidemiology and economic impact of HCUs is not well understood. Most interventional studies have focused on case management, care coordination and disease management of high-risk or high-needs patients with the aim of preventing ED visits and hospitalizations.(6) However, it is unclear whether these interventions significantly improve clinical outcomes, decrease healthcare utilization and/or reduce healthcare expenditures: they have had mixed and inconsistent results, and the overall quality of evidence is low using the GRADE criteria.(6,7)

One of the primary challenges has been determining which patients, co-morbidities, medications and healthcare services are most likely to benefit from intervention and identifying the key elements of a successful strategy. A recent analysis of HCUs in Ontario suggested that improved management of HCUs would require different tactics for different HCU sub-populations due to causes and solutions that vary by age and context.(8) Older adults aged 65 years and older account for the largest proportion of HCUs and they arguably represent the most important HCU sub-population to target.(9) However, studies focused specifically on older adult HCUs are sparse. We have previously described their unplanned hospitalizations as well as the incremental and regional variation of their healthcare costs.(10–12) The impact of medication costs and the quality of prescribing on HCU development remains unclear. The prevalence of potentially inappropriate

prescribing is reported to be 21-79% in the general older adult population and it is likely higher in the older adult HCU given higher rates of polypharmacy.(13)

Planning interventions and developing effective health policy for older adult HCUs requires a deeper understanding of their demographics, co-morbidities, medications, healthcare providers, and their health service utilization and associated costs compared to others. To address these knowledge gaps, we will be conducting the **HI**gh cost user **C**haracterization of **O**ntario's **S**eniors' medica**T**ion use and healthcare u**T**ilization (HiCOSTT) study.

Study Objectives

The primary objective of this study is to determine the relative financial and clinical contributions of prescription medications on healthcare system expenditures and the development of incident HCU status in older adults. The secondary objective is to characterize how the clinical profiles and prognoses of older adult HCUs differ from non-HCUs by describing their socio-demographics, co-morbidities, health service use, medication use, clinical outcomes, and healthcare expenditures. The main research questions, hypotheses and outcomes are described in Table 1. By exploring health service and medication utilization patterns during the transition period from non-HCU to HCU, we seek to identify opportunities to improve the quality of care and prevent HCU development. This may include the development of new health-related policies or targets for intervention, such as specific high-risk patients suited for more intensive transitional care programs or high-cost drugs suited for reference-based drug pricing reimbursement.

METHODS

Study Design

This is a retrospective population-based matched cohort study that is registered with clinicaltrials.gov (NCT02815930). A case-control study design is being concurrently used to discriminate the impact of specific medication classes on the development of HCU status. This protocol is reported with guidance from the REporting of studies Conducted using Observational Routinely collected health Data statement for PharmacoEpidemiology (RECORD-PE) checklist.(14)

Observational Periods

The observational study period will run from April 1, 2010 to March 31, 2014. The accrual period to ascertain exposure (i.e. HCU status) will extend from the index date of April 1, 2013 to the maximum follow-up date of March 31, 2014. This will allow for a 1-year look-back period to determine incident HCUs, baseline demographics, and medication and health services utilization data prior to HCU status as well as a 3-year look-back period to determine co-morbidities.

Participants

The study population is incident older adult HCUs aged 66 years or older with annual total healthcare expenditures within the top 5% threshold of all residents in the province of Ontario, Canada (estimated to be ~$8,000 annually in 2011).(8) This top 5% financial threshold will be determined using the ICES person-level health utilization costing algorithms.(15) Total expenditures associated with all healthcare utilization for each eligible Ontario resident in the fiscal year will be calculated. Individuals will then be sorted by healthcare expenditures to identify the 5% of HCUs.

Inclusion and Exclusion Criteria:

Patients will be included if they: (1) were Ontario residents registered in the Ontario Health Insurance Plan (OHIP) Registered Persons Database (RPDB) during the accrual period, (2) aged 66 years or older on the index date of April 1, 2013. Patients will be excluded if they: (1) do not have a valid OHIP number or (2) died on or prior to the index date.

Study cohort selection is shown graphically in Figure 1. The **"prevalent HCU"** cohort will be defined as those patients who had annual total healthcare expenditures in the accrual period equal to or greater than the top 5% financial threshold for fiscal year 2013 (FY2013). The **"incident HCU"** cohort will be defined as those patients in the prevalent HCU cohort whose annual total healthcare expenditures in FY2012 did not meet the top aforementioned 5% financial threshold. The **"non-HCU"** cohort will be defined as those patients whose annual total healthcare expenditures were less than the top 5% financial threshold in both FY2012 and FY2013.

The incident HCU cohort will be matched to a cohort of non-HCUs using a 3:1 matching ratio (non-HCU to HCU) based on age at cohort entry (+/- 1 month), sex and geographic location of residence for comparative analysis. The geographic location of residence will be based on Local Health Integration Networks (LHINs), which are the health authorities responsible for regional administration of public healthcare services in the province of Ontario, Canada.

The creation and matching of these cohorts in this fashion was conducted in order to: (1) focus on incident HCU patients (rather than those transitioning out of HCU status or remaining as HCUs) and (2) include as many incident HCUs as possible to look for important cohort and subgroup characteristics (i.e. co-morbidities, drug use, healthcare utilization), while minimizing confounding due to age, gender and geography. The 3:1 matching ratio was selected to minimize risk of bias by confounding and increase our statistical efficiency.(16)

Databases Used

Individual patient-level data will be obtained from ICES, which holds linked health administrative databases for the Ontario population covered by the publicly-funded provincial health care services program. These databases are linked using patient-specific, coded identifiers. This study will use 19 health administrative databases to track all health service encounters such as physician billings, hospitalizations, and prescription drugs. These specific databases and their contents are described in Table 2.

Study Outcomes

Study outcomes are summarized in Table 1. The primary outcomes of the study are the between-group (incident HCU versus non-HCU) differences of the following in the one year period after the index date: (1) the annual total prescription medication expenditures per patient and (2) the annual drug cost to total healthcare expenditure ratio. The secondary outcomes of the study are the between-group differences in the one-year (1) all-cause mortality rate and (2) all-cause hospitalization rate.

All-cause mortality will be determined using records from the OHIP RPDB. All-cause hospitalization rate will be determined by dividing the frequency of patients admitted to hospital by the total number of days patients were not hospitalized (i.e. days at risk) during the given year. A "hospitalization" will be defined as each unique "episode of care." An episode of care links a series of admissions to acute care hospitals when a patient is transferred from one hospital to another in order to prevent transfers being counted as a hospital readmission.

Data Analysis

Descriptive statistics (e.g. mean and standard deviations, medians and inter-quartile ranges, counts and percentages) will be used to describe the study cohorts and outcomes. The standardized difference will be used to compare the distribution of baseline covariates between groups for the matched cohort. A standardized difference greater than 0.1 will be interpreted as representing a meaningful difference.(17) Data cell sizes containing fewer than five counts will not be reported to protect confidentiality as per standard ICES procedures.

Baseline characteristics of the HCU and non-HCU cohort will be obtained including socio-demographics (e.g. age, gender, income quintile, social assistance recipient, immigration status), geographic distribution (e.g. health region, rurality) and exposure to primary care. Geographical rurality will be defined by the Rurality Index of Ontario (RIO) score where urban, suburban and rural will be defined by RIO scores of <10, 10-39, and ≥40 respectively. A patient will be considered a recent immigrant if they landed in Canada less than 15 years from the index date according to the Citizen and Immigration Canada (CIC) database. A patient's exposure to primary care will be characterized based on whether they have an identified primary care provider in the Client Agency Enrolment Program (CAPE) database and the associated payment model for that provider. These payment models include fee-for-service (FFS), enhanced FFS, Family Health Team (FHT), and capitation (CAP) models.

The comorbidity burden of each cohort will be summarized by using the John Hopkins Adjusted Clinical Groups (ACGs). The ACG system assigns International Classification of Diseases (ICD) diagnosis codes from inpatient and ambulatory health administrative data to one of 32 diagnosis clusters known as Aggregated Diagnosis Groups (ADGs). Previous studies have shown that ADGs can be used to accurately predict 1-year mortality in a general population

cohort.(18) Co-morbidities will be profiled by focusing on the most prevalent, clinically important or economically important disease states identified by John Hopkins Expanded Diagnosis Clusters (EDCs). Based on the ACG System, EDCs are groupings of diagnostic codes that describe the same or related condition.

In the incident year and year prior to becoming a HCU, drug and healthcare utilization of both cohorts will be delineated to compare and contrast how healthcare resources are being used by older adult HCUs and non-HCUs. This will include annual usage rates of emergency departments, hospitals, physician visits and home care services. Reasons for hospitalization will be determined using the ICD codes on the discharge abstract. Healthcare expenditures will also be broken down into key components (e.g. hospitalization, long-term care, home care, drugs, etc.) as per the ICES costing algorithm.(15) Similar analyses will be conducted in the year of incident HCU designation and for non-HCUs.

Identification of the most commonly used therapeutic medication classes and the most common reasons for hospitalizations will be used to hypothesize care management issues that may be contributing to HCU development. For example, the prevalent use of specific medication classes will be cross-referenced with the chronic co-morbidity profiles of these cohorts to explore the clinical appropriateness and financial implications of current drug utilization by (1) HCUs vs. non-HCUs and (2) HCUs pre- vs. post-HCU designation.

Medication classes of interest have been selected a priori for analysis based on consideration of: (1) those with a strong evidence base for the prevention of complications of common, high priority disease states in older adult ("high quality" medications), (2) those with a strong evidence base for harms outweighing potential benefits or those commonly targeted for deprescribing in older adults due to potential inappropriateness [e.g. sedative-hypnotics,

antipsychotics, opioids] ("high risk" medications), and (3) those known to be high cost (per unit) medications (Table 3).(19,20) Use of these medications, defined as the occurrence of prescription claims for them during the study period, will be described descriptively.

Using a case-control study design with HCU development as an outcome, logistic regression analyses will be conducted to explore the relationship between the use of these medications and future incident HCU status. In order to control for potential bias including confounding by indication and severity of illness, estimates will be adjusted for age, sex, number of co-morbidities, number of major John Hopkins ADGs and co-morbidities with possible indications for the drug(s) of interest. This data will be used to explore whether more in-depth analysis is required (i.e. are there signals that there are potential drug-related interventions prior to HCU designation that could be implemented to avoid critical healthcare events, minimize drug-related expenditures and/or prevent HCU status).

INTERPRETATION

Comparative analysis of drug and healthcare utilization and expenditures during the HCU transition period will help identify key contributors to HCU development. We expect to find common groups of diagnoses, medications and clinical outcomes amongst older adult HCUs. Some of these conditions may be amenable to cost-effective preventative management strategies or less expensive, but equally effective medication therapies. In particular, this study's data will confirm whether or not prescription drug costs represent a significant proportion of overall healthcare costs, how medication and healthcare expenditures change with HCU status and whether there is a gap in the appropriate and cost-effective use of prescription medications. This will facilitate: (1) the identification of potential high-yield areas for targeted clinical or medication

management interventions to prevent HCU development, (2) provision of data to support health policies for HCUs in Ontario, and (3) areas requiring further study.

Ethical Approval

This study was approved by the Hamilton Integrated Research Ethics Board (HiREB).

Strengths and Limitations

To our knowledge, this is one of the first population-based matched cohort analyses of older adult HCUs and their medication use. Utilization of linked health data in a large population of older adults (n=5,352,983) provides a unique opportunity to compare and contrast characteristics of HCUs to their non-HCU counterparts.(21) The focus on the incident rather than prevalent HCUs allows for identification of potential triggers of HCU status and exploration of potential preventative interventions. The large estimated cohort size makes it possible to study predictors of high cost healthcare use amongst older adults with statistical efficiency and determine their impact on clinical outcomes that transcend differences in local practice patterns. Access to medication records from the ODB plan provides drug data that is generally more accurate than self-recorded information on drug use.

This study is subject to the limitations and residual confounding inherent in observational data from health administrative databases. It is not possible to guarantee that patients were adherent to the dispensed medications nor that they were used appropriately as prescribed. Second, co-morbidity and disease data are reliant on the use of hospital discharge diagnosis data using ICD and billing codes. Although the quality of discharge coding is generally good, we do not know the accuracy of each and every diagnosis listed on a discharge abstract.(22) Physicians are also

permitted only one diagnosis code for each office encounter. This means that acute problems often take precedent over chronic ones, which can serve to under-represent the prevalence of chronic disease.

Conclusion

This study will determine the relative contribution of medications to HCU expenditures and explore whether the quality of prescribing and medication use may be contributing to suboptimal clinical outcomes and their high cost use. By identifying key contributors to HCU status, we will help clinicians, administrators, and policy makers determine which patients, diseases, drugs and expenses could benefit from intervention. If modest improvements in prescribing and medication use can be achieved, then there will likely be significant healthcare savings that could be re-invested to fund better care for these high-risk, high-cost older adults.

Author Contributions:

JL, AH, SM, JET, JMP and KT conceptualized the study. All authors contributed to its design. JL drafted the initial protocol manuscript and all authors contributed to revision and final approval.

Funding Statement

This work is supported by the Ontario Drug Policy Research Network (ODPRN) which is funded by grants from the Ontario Ministry of Health and Long-Term Care, and the Ontario Strategy for Patient-Orientated Research (SPOR) Support Unit, which is supported by CIHR and the Province of Ontario. This study will also be supported by the Institute for Clinical Evaluative Sciences (ICES), which is funded by an annual grant from the Ontario Ministry of Health and Long-Term

Care, and by personnel funding from the Canadian Institute of Health Research (CIHR) Fellowship Program, the CIHR Drug Safety and Effectiveness Cross-Disciplinary Training (DSECT) Program, the Research Institute of St. Joe's Hamilton, and the St. Peter's/McMaster Chair of Aging. The opinions and conclusions reported in this article are those of the authors and are independent from the funding sources. No endorsement by ICES or the Ontario MOHLTC is intended or should be inferred.

Competing Interests

None declared.

REFERENCES

1. Blair A, Baigent L. High Cost Users. In: Presented at: MOHLTC Transformation Secretariat Meeting – Understanding Ontario's high cost health care users. Toronto, ON; 2013.
2. Ontario Ministry of Finance. Ontario Population Projections Update, 2012–2036. [Internet]. 2012 [cited 2014 Oct 12]. Available from: http://www.fin.gov.on.ca
3. Calver J, Brameld KJ, Preen DB, Alexia SJ, Boldy DP, McCaul KA, et al. High-cost users of hospital beds in Western Australia: A population-based record linkage study. Med J Aust. 2006;184(8):393–7.
4. National Institute for Health Care Management. The Concentration of Health Care Spending. Washington, DC; 2012.
5. Bardsley M, Lewis G. Reflections from the NHS in England. Healthc Pap. 2014;14(2):26–30.
6. Lee J, Muratov S, Tarride J-E, Holbrook A. Managing High-Cost Healthcare Users: The International Search for Effective Evidence-Supported Strategies. J Am Geriatr Soc. 2018;66(5):1002–8.
7. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol. 2011 Apr;64(4):383–94.
8. Wodchis WP, Austin PC, Henry DA. A 3-year study of high-cost users of health care. CMAJ. 2016 Jan 11;188(3):182–188.
9. Wodchis WP. The Concentration of Health Care Spending: Little Ado (yet) About Much (money) [Internet]. 2012 Canadian Association for Health Services and Policy Research

Conference. Montreal, QC; 2012 [cited 2015 Oct 1]. Available from: https://www.cahspr.ca/web/uploads/presentations/C6.1_Walter_P._Wodchis.pdf

10. Muratov S, Lee J, Holbrook A, Paterson JM, Guertin JR, Mbuagbaw L, et al. Unplanned index hospital admissions among new older high-cost health care users in Ontario: a population-based matched cohort study. C Open. 2019 Jul 25;7(3):E537–45.

11. Muratov S, Lee J, Holbrook A, Guertin JR, Mbuagbaw L, Paterson JM, et al. Incremental healthcare utilisation and costs among new senior high-cost users in Ontario, Canada: a retrospective matched cohort study. BMJ Open. 2019 Oct 28;9(10):e028637.

12. Muratov S, Lee J, Holbrook A, Costa A, Paterson JM, Guertin JR, et al. Regional variation in healthcare spending and mortality among senior high-cost healthcare users in Ontario, Canada: a retrospective matched cohort study. BMC Geriatr. 2018 Dec 1;18(1):262.

13. Hill-Taylor B, Sketris I, Hayden J, Byrne S, O'Sullivan D, Christie R. Application of the STOPP/START criteria: A systematic review of the prevalence of potentially inappropriate prescribing in older adults, and evidence of clinical, humanistic and economic impact. J Clin Pharm Ther. 2013;38(5):360–72.

14. Langan SM, Schmidt SA, Wing K, Ehrenstein V, Nicholls SG, Filion KB, et al. The reporting of studies conducted using observational routinely collected health data statement for pharmacoepidemiology (RECORD-PE). BMJ. 2018 Nov 14;363:k3532.

15. Wodchis WP, Bushmeneva K, Nikitovic M, McKillop I. Guidelines on person-level costing using administrative databases in Ontario. 2013;1(May):1–71.

16. Breslow N, Day N. The Analysis of Case-Control Studies. In: Statistical Methods in Cancer Research. Lyon, France: International Agency for Research on Cancer; 1980. p.

169.

17. Austin P. Using the standardized difference to compare the prevalence of a binary variable between two groups in observational research. Comm Stat Simul Comput. 2009;38(6):1228–34.

18. Austin PC, van Walraven C, Wodchis WP, Newman A, Anderson GM. Using the Johns Hopkins Aggregated Diagnosis Groups (ADGs) to predict mortality in a general adult population cohort in Ontario, Canada. Med Care. 2011 Oct;49(10):932–9.

19. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing. 2015;44(2):213–8.

20. Deprescribing.org. Deprescribing Guidelines and Algorithms [Internet]. [cited 2019 Mar 3]. Available from: https://deprescribing.org/resources/deprescribing-guidelines-algorithms

21. Statistics Canada. Table 17-10-0005-01 Population estimates on July 1st, by age and sex (2013) [Internet]. [cited 2019 Sep 15]. Available from: https://doi.org/10.25318/1710000501-eng

22. Juurlink D, Preyra C, Croxford R, Chong A, Austin P, Tu J, et al. Canadian Institute for Health Information Discharge Abstract Database: A Validation Study [Internet]. ICES Investigative Reports. Toronto, ON; 2006 [cited 2019 Oct 1]. Available from: https://www.ices.on.ca/Publications/Atlases-and-Reports/2006/Canadian-Institute-for-Health-Information

Table 1: Main Research Questions, Hypotheses and Outcome Measures

Main Research Questions	Hypotheses	Study Design	Main Outcome Measures
Primary			
What is relative financial contribution of prescription medications to HCU status?	• Prescription medication costs will rank within the top 3 cost categories of HCU expenditures • In a subset of incident HCUs, prescription medication costs alone will be greater than the financial threshold for HCU status	Retrospective Matched Cohort Analysis (HCU status treated as an 'exposure')	• Annual total prescription medication costs • Annual drug cost to total healthcare expenditure ratio • Frequency of patient cases where annual drug costs alone exceeds health expenditure threshold for HCU status
What is the relative clinical contribution of prescription medications to incident HCU status? Does the quality of medications prescribed and used contribute to HCU development?	• The use of "high quality" medication classes (i.e. those with a strong evidence base for primary or secondary prevention selected a priori for analysis) will be associated with a decreased odds of incident HCU status • The use of "higher cost (per unit)" medications and "potentially inappropriate/high risk" medications selected a priori for analysis will be associated with an increased odds of incident HCU status	Case-Control Analysis (HCU status treated as an outcome)	• Odds ratio of incident HCU status
Secondary			
What is the relative difference in clinical profiles of newly incident HCUs vs. non-HCUs	• Incident HCUs will have a significantly higher annual risk of mortality and hospitalizations compared to non-HCUs	Retrospective Matched Cohort Analysis	• All-cause mortality rate • All-cause hospitalization rate • Number of John Hopkins Adjusted Diagnostic Groups

including comorbidities, medications, and prognosis?	• Incident HCUs will have a significantly higher prevalence and baseline burden of co-morbidities and prescription drug use compared to non-HCUs	(HCU status treated as an 'exposure')	[ADGs] and Expanded Diagnosis Clusters [EDCs] • Number of unique prescription drug classes dispensed
What is the prevalent use of prescription medication classes with a strong evidence base for primary or secondary prevention of complications associated with the most common chronic conditions?	• The prevalent use of "high quality" prescription medication classes will be lower in HCUs compared to non-HCUs with the relevant associated co-morbidities in the pre-HCU year	Retrospective Matched Cohort Analysis (HCU status treated as an 'exposure')	• Prevalent use of "high quality" medication classes selected a priori for analysis • Prevalence of relevant chronic condition based on John Hopkins Expanded Diagnosis Clusters [EDCs] and chart-validated ICES chronic disease cohorts

Table 2: Health Administrative Databases

Health Administrative Database	Description	Database Variables/Data Used
Ontario Registered Persons Database (RPDB)	The Ontario Registered Persons Database (RPDB) records vital statistics, including date of death.	• Date of death • Rurality Index Ontario Score • Age • Sex
Citizenship and Immigration Canada (CIC) Database	The Citizenship and Immigration Canada (CIC) Database contains landing records for every permanent legal immigrant to Canada who arrived from 1985 onward.	• Date of landing/immigration
Local Health Integration Network (LHIN) database	The Local Health Integration Network (LHIN) database contains records the health authorities responsible for the regional administration of public healthcare services in the province of Ontario, Canada.	• Geographic location of residence of included patients
Ontario Drug Benefit (ODB) database	The Ontario Drug Benefit (ODB) database contains highly accurate records for outpatient prescriptions dispensed to patients aged 65 years or older (with error rates reported to be less than 1%).	• Prescription drug fill dates and costing • Long-term care indicator
Canadian Institute for Health Information–Discharge Abstract Database (CIHI-DAD)	The Canadian Institute for Health Information–Discharge Abstract Database (CIHI-DAD) contains patient-level demographic, diagnostic, procedural and treatment information on all acute care hospitalizations.	• ICD-10 Codes for Hospital Discharge Diagnoses and John Hopkins ACGs and EDCs • Hospitalizations (elective and urgent) and costing
CIHI—National Ambulatory Care Reporting System (CIHI-NACRS) database	The CIHI—National Ambulatory Care Reporting System (CIHI-NACRS) database contains patient-level demographic, diagnostic, procedural and treatment information for all hospital-based and community-based ambulatory care including day surgery, outpatient and community-based clinics, and emergency departments.	• ICD-10 Codes for Hospital Discharge Diagnoses and John Hopkins ACGs and EDCs • Visits and costing

CIHI-Same Day Surgery (SDS)	The CIHI-Same Day Surgery (SDS) contains patient-level demographic, diagnostic, procedural and treatment information on all day surgeries.	• ICD-10 Codes for Hospital Discharge Diagnoses and John Hopkins ACGs and EDCs • Visits and costing
CIHI-National Rehabilitation Reporting System (NRS)	The CIHI-National Rehabilitation Reporting System (NRS) contains patient-level demographic, diagnostic, procedural and treatment information from participating adult inpatient rehabilitation facilities and programs.	• Visits and costing
Ontario Home Care Database (HCD)	The Ontario Home Care Database (HCD) contains patient-level demographic, diagnostic, procedural and treatment information on all home care visits.	• Home care visits • Type of home care service provided • Visits and costing
Ontario Continuing Care Reporting System (CCRS)	The Ontario Continuing Care Reporting System (CCRS) contains demographic, clinical, functional and resource utilization information on individuals receiving continuing care services in hospitals or long-term care homes in Canada.	• Visits and costing
Ontario Mental Health Reporting System (OMHRS) database	The Ontario Mental Health Reporting System database contains patient-level demographic, diagnostic, procedural and treatment information on all psychiatric facility visits.	• Visits and costing
ICES Physician Database (IPDB)	The ICES Physician Database (IPDB) which reports prescriber and specialist referral data in Ontario.	• Visits to primary care and specialists
Ontario Health Insurance Plan database (OHIP)	The Ontario Health Insurance Plan database (OHIP) which includes health claims for physician services.	• ICD-10 Codes for Hospital Discharge Diagnoses and John Hopkins ACGs and EDCs • All health service visits and costs
Client Agency Program Enrolment (CAPE) database	The Client Agency Program Enrolment (CAPE) database contains enrolment information of an individual in a	• Primary care practitioner

	programme with a specific practitioner and group.	reimbursement model of included patients
ICES-derived cohorts: • Congestive Heart Failure (CHF) database • Chronic Obstructive Pulmonary Disease (COPD) database • Ontario Crohn's and Colitis Cohort Database (OCCD) database • Ontario Diabetes Database (ODD) • Ontario Myocardial Infarction Database (OMID) database • Ontario Rheumatoid Arthritis Database (ORAD) database	The ICES-derived cohorts are chart-validated cohorts of individuals with specific diseases and conditions.	• Co-morbidities of included patients

Table 3: Medication Classes of Interest for Patient-Level Analysis

High Quality Medication Use	Potentially Inappropriate/ High Risk Medication Use	High Cost Drug Use
• Statins • Beta-blockers • ACE inhibitors • ARBs • Angiotensin II combination • ACE inhibitors combination • Vitamin K Antagonists • NSAIDs (ASA) • Anticoagulants (DOACs) • Anticoagulants (miscellaneous) • Bisphosphonates • Bone calcium regulator (Denosumab) • Bronchodilator and anti-inflammatory combination • Anti-cholinergics (Tiotropium, Ipratropium)	• Proton pump inhibitors • Benzodiazepines • Narcotics: Opiate Agonists • Antipsychotics • NSAIDs (non-ASA) • Digitalis Preparations (Digoxin)	• Immunosuppressive agents (Mycophenolic acid, natalizumab, sirolimus, tacrolimus, thalidomide) • Antineoplastic agents (e.g. tocilizumab, imatinib, dasatinib) • Opthalmologicals (Ranibizumb) • Biologic Response Modifying Agents (Adalimumab, aldesleukin, certolizumab, etanercept, glatiramer, golimumab, infliximab, interferons, levamisole)

Figure 1: Study Cohort Selection