INCIDENT SENIOR HIGH-COST HEALTHCARE USERS IN ONTARIO

CHARACTERIZATION OF INCIDENT SENIOR HIGH-COST HEALTHCARE USERS IN ONTARIO: POLICY AND RESEARCH IMPLICATIONS

BY

SERGEI MURATOV MD, MPH

A Thesis Submitted to the School of Graduate Studies in Partial Fulfilment of the Requirements for the Degree Doctor of Philosophy

McMaster University DOCTOR OF PHILOSOPHY (2019) Hamilton, Ontario (Health Research Methodology – Health Technology Assessment Specialization)

TITLE: Characterization of Incident Senior High-Cost Healthcare Users in Ontario: Policy and Research Implications

AUTHOR: Sergei Muratov, MD (Karaganda State Medical University, 2000), MPH (Boston University, 2005)

SUPERVISOR: Associate Professor Dr. Jean-Eric Tarride

NUMBER OF PAGES: xiv; 150

LAY ABSTRACT

A small group of patients that use the most of healthcare resources are called high-cost users (HCU). HCUs are often seniors. Policy makers need a better understanding of new senior HCUs to be able to prevent seniors from becoming HCU. This study used administrative data and advanced statistical methods. We found that almost one-tenth of the 2013 provincial healthcare budget was spent on new senior HCUs, mainly because of lengthy unplanned hospitalizations. Patients who lived in long-term care, had a primary care provider, or recently visited a geriatrician were less likely to have an unplanned hospitalization. Overall, healthcare costs were distributed equally to Ontario seniors, but access to healthcare services varied greatly. This variation could not be explained by differences in age, sex, or health status. This thesis advances our knowledge of HCUs in Canada. Additional research is needed into care associated with becoming HCU and provincial variation in accessing healthcare.

ABSTRACT

Background and Objectives: High-cost health care users (HCU) represent a minority of patients who consume a large proportion of health care resources. Due to their high burden on the healthcare system and internal heterogeneity, a better understanding of various segments of the HCU population is needed. The general objective was to advance our understanding of incident senior HCUs in the Canadian context so that we can advise health policy makers on potential strategies to prevent seniors transitioning to HCU and to identify priorities for further investigation.

Methods: A retrospective population-based matched cohort study was conducted using province-wide linked administrative data. The research employed a spectrum of advanced methods to accomplish the general objective, including the method of recycled predictions, random intercept two-part multi-level models, and stratified logistic regression.

Results: Total costs attributable to incident senior HCU status accounted for almost one-tenth of the provincial healthcare budget, with prolonged hospitalizations making a major contribution. Unplanned first (index) hospitalizations (IHs) in the incident year were considerably more common among HCUs, with ten conditions accounting for one third of their total costs. A lower risk of IH among HCUs was associated with residence in long-term care (LTC), attachment to a primary care provider, and recent consultation by a geriatrician. Although there was little variation in costs incurred by Ontario seniors for healthcare services they receive, access to the healthcare services varied greatly. The traditional drivers of costs and mortality (e.g., age, sex, health status) played little role in driving the observed variation in HCUs' outcomes.

Conclusions: By answering research questions, this thesis advances our knowledge of the HCU population in Canada. Further exploration of the nature and quality of care that may be associated with HCU conversion and investigation of the regional variation in accessing specific healthcare services is warranted.

ACKNOWLEDGMENTS

The journey to my PhD would not be possible without a few special people. I am immensely grateful to my supervisor, Dr. Jean-Eric Tarride, for his outstanding support, guidance, and mentorship, for making my success his highest priority, sharing his technical expertise, and, of course, his keeping a positive attitude no matter what challenges we were faced with.

Many thanks go to my dearest PhD Committee members. I would like to thank Dr. Anne Holbrook for her overall support, for encouraging me to think further and beyond what would seem as a decent solution, and for sharing opportunities for personal growth. I am very much grateful to Drs. Jason Guertin and Lawrence Mbuagbaw for their continuous support, guidance and simply being good friends: not once did I come with a question for them that they never took long to provide help on.

It was a real pleasure to collaborate with Team ICES (Michael Paterson, Dr. Tara Gomes, Priscila Pequeno, Wayne Khuu, Jun Guan, Jiming Fang, Alex Kopp): a fantastic body of knowledge and a wealth of expertise that propel analytical work to the new heights of quality standards.

I would like to express my sincere gratitude to HRM Staff and students that I have come in contact with during my journey for being so supportive and helpful.

Last but so not least, my special thanks and loving hugs go to my wife, Yuliya, and sons, German and Michael, who made this journey even more meaningful and to my parents who supplied ample encouragement and support.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

PREFACE

This is a sandwich thesis that combines 4 manuscripts prepared for publication in peer-reviewed journals. The first two have been published. The following are contributions of Sergei Muratov in all the papers included in this thesis: developing the research questions,

writing the protocol and statistical analyses plans, conducting statistical data analyses; designing the figures; writing all the manuscripts; submitting the manuscripts and responding to reviewers' comments. My co-authors contributed in acquiring data and reviewing the manuscripts prior to publication. The work in this thesis was conducted between Winter 2016 and Fall 2018.

LIST OF ABBREVIATIONS

ACGs - Johns Hopkins Adjusted Clinical Groups

ACSC – Ambulatory care sensitive conditions

ADGs - Johns Hopkins Aggregated Diagnosis Groups

ALC – Alternate level of care

ALOS – Acute length of stay

BC- British Columbia, Canada

CAD – Canadian dollar

CCC - Continuing Complex Care

CI – Confidence interval

CHF - Congestive heart failure

COPD - Chronic obstructive pulmonary disease

CV – Coefficient of variation

DM- Diabetes

DID – Difference in differences

ED – Emergency Department

EDCs - John Hopkins Expanded Diagnosis Clusters

EQ – Extremal quotient

FFS – Fee for service

FHN – Family Health Network

FHO – Family Health Organization

FHT – Family Health Team

FY – Fiscal year

GLM - Generalized linear models

GMD – Gini mean difference

GP – General practitioner

HCU – High-cost user

ICC – Intra-class correlation coefficient

ICD – International Statistical Association of Diseases and Related Health Problems

IH – Index (first) hospitalisation

LHIN - Local Health Integration Networks

LRT – Likelihood ratio test

LTC - Long-term care

MI- Myocardial infarction

MOHLTC – Ministry of Health and Long-term care

MRDX – Major diagnosis code responsible for resource use

NB – Negative binomial

OECD - Organization for Economic Cooperation and Development

ODB - Ontario Drug Benefit

RA- Rheumatoid arthritis

RIO - Rural Index of Ontario

QGIS - Quantum geographic information system

SD – Standard deviation

SDD – Absolute Standardized difference

TLOS – total length of stay

Chapter 1

INTRODUCTION

When Roemer et al. (Canada) and Densen et al. (USA) published their research on frequently hospitalized patients in Saskatchewan and high utilizers of physician services in New York in 1956 and 1959, respectively, they could not foresee that several generations to come health policy makers and researchers would still be pre-occupied with very similar issues (Densen, Shapiro, & Einhorn, 1959; Roemer & Myers, 1956). Densen et al. state in their introduction "...studies have demonstrated repeatedly that small groups account for disproportionately large shares of the adverse events experienced by the population…" and continue "thus, the uneven distribution of medical costs in the population has spurred much of the interest in the extension of health insurance to all types of physician services". Although one the earliest published accounts of the phenomenon, this statement suggests that the issue had been researched prior to their study and this phenomenon was already well known. Whether these patients are called heavy users, high utilizers, frequent users, or high-cost users (HCU), the concept implied is the same: a small group of people accounts for a large share of healthcare resources consumed. Presently, the most common approach to defining HCUs is to describe cost concentration by percentiles of the population (Wammes, van der Wees, Tanke, Westert, & Jeurissen, 2018). In Canada, HCUs are typically referred to as the top 5% most costly patients (Fitzpatrick et al., 2015; Rais et al., 2013; Reid et al., 2003; Wodchis, Austin, & Henry, 2016).

There are several reasons why researchers have maintained their interest in such an "ancient" topic as HCU. First, it is hoped that optimal management of these patient subpopulations will help reduce healthcare costs (Holtz-Eakin, 2005; Wammes et al., 2018). Led by the US, healthcare spending has more than doubled across the countries of the Organization for Economic Cooperation and Development (OECD) over the past two decades (World Health Organization, 2018). In Canada, where public health and health care are under provincial jurisdiction, health spending accounts for 37% of the total provincial program spending on average (Canadian Institute for Health Information, 2017). The number of studies on HCUs in Ontario has greatly increased in recent times prompted by the economists' worries about provincial healthcare funding sustainability (Wammes et al., 2018). Second, Densen et al. and Roemer et al. had study populations of approximately 20,000 subjects and employed data analysis of a few variables that was largely descriptive. Lately, a massive amount of provincial-level healthcare administrative data has become increasingly available for researchers. Coupled with rapidly growing computational capacity, this offers new opportunities for advanced analytics in support of policy making. Third, there is a sense within the research community that important aspects related to HCU characteristics and care have not been adequately described, especially in Canadian settings.

HCUs are a heterogenous group that includes premature or disabled neonates, trauma patients, socially disadvantaged individuals, and seniors with multiple comorbidities. Therefore, interventions need to be tailored to specific HCU population segments (Blumenthal, Chernof, Fulmer, Lumpkin, & Selberg, 2016). Recently, a series of Canadian studies have shed light on the characteristics of HCUs in general (C. de Oliveira, Cheng, Vigod, Rehm, & Kurdyak, 2016; Fitzpatrick et al., 2015; Guilcher, Bronskill, Guan, &

Wodchis, 2016; Hensel, Taylor, Fung, & Vigod, 2016; Rais et al., 2013; Rosella et al., 2014; Wodchis et al., 2016). Some of them focused on HCUs with mental health issues (C. de Oliveira et al., 2016; Hensel et al., 2016) but none have focused on seniors. In fact, a typical Canadian senior HCU has not yet been well described. This is surprising as seniors account for 46% of the national public healthcare expenditures in Canada (Canadian Institute for Health Information, 2017). This proportion is likely to increase due to the continued ageing of the population, therefore putting additional pressure on the government's resource allocation decisions in the coming years. Also, the majority of HCUs are seniors: for example, 60% of all HCUs in Ontario, Canada's most populous province (Rais et al., 2013). Consistent with findings from other jurisdictions (Central Midlands NHS, 2014; Stanton MW, 2006), a recent Ontario study showed that 5% of senior HCUs consume 44% of the total measured public healthcare expenditures by the seniors in the province (Wodchis et al., 2016).

Research efforts targeting senior HCUs are a priority given that the effectiveness of interventions aimed at HCUs, including seniors has not been confirmed. We recently reviewed international studies on this topic and concluded that there is no solid evidence of effectiveness or cost-effectiveness among them (J. Y. Lee, Muratov, Tarride, & Holbrook, 2018). Moreover, a recent evaluation of the initial results of the Ontario provincial Health Links initiative (mean age of the enrolees: 74.6 years; standard deviation (SD): ±13.9) also revealed no effect on hospital admissions among high-needs patients (Mondor, Walker, Bai, & Wodchis, 2017).

One approach to further clarify senior HCU characteristics and needs is population segmentation (Blumenthal et al., 2016; J. Y. Lee et al., 2018). Many disease management programs as well as research efforts focus on persistent HCUs, i.e., those that retain their HCU status in subsequent years (Nelson, 2012; Peikes, Chen, Schore, & Brown, 2009; Wodchis et al., 2016). However, incident (or "new") HCUs have historically accounted for more than 50% of all the HCU cases annually, including those among senior patients (Roos, Shapiro, & Tate, 1989; Wodchis et al., 2016). Incident senior HCUs may have different characteristics than prevalent senior HCUs, and more focus on incident HCUs would allow for scrutiny of the factors that influence the transition from non-HCU to HCU.

Most of the HCU research up until recently has employed a cross-sectional design, which is of lower quality than cohort or case-control (Fitzpatrick et al., 2015). In studies with a comparator, the typical comparison group are the patients at the 50-95th percentiles. Matching HCUs with non-HCUs however would offer a more accurate assessment of the distinguishing features of HCU status while a longitudinal assessment would also improve delineation of its drivers. In this respect, the characteristics of care provided in the pre-incident year deserve attention. Although possible socio-demographic and public health predictors of the HCU status in general have been explored (Wammes et al., 2018), there is still a lack of predictor information for the senior segment of the Canadian HCUs. Moreover, a better understanding is needed of the outpatient care provided prior to the HCU conversion (e.g. home care or physician visits) and the environment within which the care was received (e.g., primary care model) to inform interventions aimed at preventing the HCU conversion.

Importantly, HCU related research with a system-wide approach is also limited (Rais et al., 2013; Wodchis et al., 2016) as studies have largely focused on acute care (e.g. hospitalizations, emergency care, physicians) and left out other important cost categories such as long-term care or rehabilitation. This narrows our understanding of their role in the HCU conversion.

Finally, regional variation of costs across the cost categories as well as patient outcomes (e.g., mortality) have not been explored for senior HCUs. While there are some data on regional variation in healthcare expenditures from British Columbia (BC), the study focused on the entire population of the province and total costs only. Examining regional variation in both costs and outcomes across the system would allow exploration of its drivers (e.g., socio-demographic factors and health status) and the amount of variation they explain, facilitate assessment of regional equality in resource allocation, and inform cost-outcome relationships.

Thesis objective and outline:

The general objective of this thesis is to advance our understanding of incident senior HCUs in the Canadian context such that we can inform health policy making on potential strategies to prevent seniors transitioning to HCU and to identify priorities for further investigation.

This thesis is a "sandwich" of 4 papers (2 published and 2 recently submitted) with important contributions to the literature in two main domains:

a) focus on an important HCU segment, which is seniors, including new information about incident HCUs and comparisons to non-HCUs for both clinical outcomes and healthcare utilization;
b) use of advanced analytical techniques such as multilevel modeling, method of recycled prediction, and two-part models to generate results.

The following are specific **research questions** addressed by the thesis:

1. What is the one-year incremental healthcare utilization and direct financial impact on public payers of becoming an incident HCU among seniors in Ontario?
2. What is the extent of regional (health planning level) variation in healthcare utilization, costs, and mortality among senior incident HCUs compared to non-HCUs in Ontario?
3. What are the characteristics of hospital admissions and associated costs in senior incident HCUs compared to non-HCUs in Ontario?

Chapter 2 is a study protocol that summarizes the rationale for investigating the issue of incident senior HCUs overall and each of the research questions specifically (Muratov et al., 2017). It outlines an analytical plan to address the research questions and provides a brief description of key methods employed in the study. Importantly, it also provides details on the sources of data for all the variables and outcomes described in the thesis.

Chapter 3 presents a longitudinal perspective describing the dynamics in healthcare use and costs in the two cohorts across a number of care categories over 2 years: pre-incident and incident. It explores whether senior HCUs were already on the upward trajectory in terms of healthcare resource utilization before they reached the HCU status. The chapter then examines the contribution of each of the 12 total cost components in their various combinations to the HCU transition: these are the most important cost categories that capture approximately 95% of the provincial spending on individual healthcare. Using the method of recycled predictions, we calculated the incremental values of healthcare utilization (e.g., hospital admissions, healthcare practitioner visits) and costs (total and by each cost component) associated with the HCU status. We also estimated the monetary impact of the incident senior HCUs on the provincial budget.

Chapter 4 first examines the variation of senior HCUs across Ontario's health districts (LHINs) and describes in detail the baseline characteristics of both HCUs and non-HCUs (Muratov S et al., 2018). Then, using random intercept two-part multi-level models, variation in healthcare costs and mortality was assessed across LHINs cross-sectionally for the incident year and compared between the cohorts. For costs, variance estimates were obtained for all 12 cost components and total costs. In addition, this chapter looks at the cost-mortality relationship by plotting random effects for total costs against the random effects for mortality to identify "pockets" of high vs. low efficiency in the province.

Finally, **Chapter 5** begins with a comparison of the attributes of first (index) unplanned acute hospitalisation (IH) in both cohorts such as acute length of stay, alternative level of care, discharge destinations, and in-patient mortality. It also identifies the top most costly causes of IHs by cohort: ICD10-CA diagnosis codes most responsible for resource use were used to identify the causes. Stratified logistic regression was then run to examine socio-demographic, health status and healthcare predictors of IHs in the pre-incident year in each cohort.

Methodological advancements to highlight:

The thesis uses a variety of advanced statistical methods to address the research questions and ensure validity of the results. First, the senior HCUs were matched to non-HCUs at a ratio of 1 HCU to 3 non-HCU on age, sex and LHIN, which allows meaningful comparisons by creating comparable groups and improves statistical efficiency of estimation (Mandrekar JN & SJ, 2004). Compared with other ratios (e.g., 1: 4 or 1:5), using the 1:3 ratio is considered very efficient, with only marginal improvements in relative efficiency beyond 3 matched controls per case (Mandrekar JN & SJ, 2004). Second, to deal with the problem of excess zeros due to the non-consumption of healthcare resource use, the analyses of costs include two-part regressions models. In two-part models, the first part assesses the probability of costs >0$ through logistic regression whereas the positive costs are fit using a generalized linear model assuming gamma distribution. This allows for a better model fit by accounting for a large mass of zero-cost observations and the typical asymmetry of cost distribution (right skew) (Gregori et al., 2011). Further, the method of recycled predictions used in Chapter 3 is an advanced approach to calculate the incremental values of healthcare resource use (Basu, Arondekar, & Rathouz, 2006; Chang et al., 2017). While comparing HCU with non-HCU, it allows to account for the correlation between outcome values in the year before the incident year and the year after and to adjust for key confounding factors. Next, statistically significant intraclass correlation coefficients across the majority of cost components and mortality in both cohorts indicated a clustering effect within LHINs and justified the use of random intercept mixed effects modelling employed in Chapter 4. This approach to assess variation is preferred to the commonly used fixed effects models where unit of variation enter the model as a dummy variable. In fixed effects models, variation assessment is then based on predicted outcome values and calculated measures of dispersion (e.g., coefficient of variation). Instead, random effects models (random intercept being the simplest option) allow for direct estimation of between-unit (LHINs) variance and for the corresponding testing of statistical hypotheses (i.e., whether the between-LHIN variation is not due to chance). Also, we used an innovative approach to present the cost-mortality relationship in both cohorts plotting the estimated random effect values for total costs vs. those for mortality in a cost-mortality plane. Finally, in Chapter 5 we used logistic regression to identify predictors of admissions. However, a more important nuance is the outcome definition: instead of examining re-admissions or all admissions as commonly done by researchers we investigated the first hospitalizations in the incident year provided that the patient had no hospital admission within 12 months before it. In summary, we have innovatively used advanced statistical methods and data analysis approaches to answer our research questions- most of these methods have never been used in the context of HCU.

Overlap in material covered:

Chapters 2-5 were developed as separate manuscripts under the same umbrella topic of incident senior HCUs using the same dataset. Therefore, some overlap exists in the Introductory, Methods, and Results sections of the manuscripts. Specific examples include the fact that study design, study setting, and cohort definitions were described similarly across all the manuscripts. Data sources were described with similar detail both in the study protocol (p.13) and Chapter 3 (p.25). Table 1 on patient baseline characteristics contains similar detail across the manuscripts (pages 37, 69, 110).

Deviation from the study protocol

We have deviated from the published protocol in two aspects. First, to assess variation we used a multi-level modelling approach and the direct variance estimate instead of a fixed effects model and measures of dispersion as described in the protocol. We modified our analytical approach in this regard after publishing the protocol in further consultations with biostatisticians and examining the role of intraclass correlation coefficient more closely. We believe this modification has improved our analysis.

Second, the component on ambulatory care sensitive conditions is still under analysis. These results have not been included in the thesis but are expected to be published at a later time once the analysis is completed.

REFERENCES

Basu, A., Arondekar, B. V., & Rathouz, P. J. (2006). Scale of interest versus scale of estimation: comparing alternative estimators for the incremental costs of a comorbidity. *Health Econ, 15*(10), 1091-1107. doi:10.1002/hec.1099

Blumenthal, D., Chernof, B., Fulmer, T., Lumpkin, J., & Selberg, J. (2016). Caring for High-Need, High-Cost Patients - An Urgent Priority. *N Engl J Med, 375*(10), 909-911. doi:10.1056/NEJMp1608511

Canadian Institute for Health Information. (2017). *National Health Expenditure Trends, 1975 to 2017*. Retrieved from Ottawa, ON: https://www.cihi.ca/en/national-health-expenditure-trends

Central Midlands NHS. (2014). *The Total Cost of Care for Older People in Solihull - an Analysis of Combined NHS and Social Care Data*. Retrieved from https://solihullccg.nhs.uk/publications/1245-bcf-cost-of-care/file

Chang, C., Lee, S. M., Choi, B. W., Song, J. H., Song, H., Jung, S., . . . Suh, D. C. (2017). Costs Attributable to Overweight and Obesity in Working Asthma Patients in the United States. *Yonsei Med J, 58*(1), 187-194. doi:10.3349/ymj.2017.58.1.187

de Oliveira, C., Cheng, J., Vigod, S., Rehm, J., & Kurdyak, P. (2016). Patients With High Mental Health Costs Incur Over 30 Percent More Costs Than Other High-Cost Patients. *Health Aff (Millwood), 35*(1), 36-43. doi:10.1377/hlthaff.2015.0278

Densen, P. M., Shapiro, S., & Einhorn, M. (1959). Concerning High and Low Utilizers of Service in a Medical Care Plan, and the Persistence of Utilization Levels over a Three Year Period. *The Milbank Memorial Fund Quarterly, 37*(3), 217-250. doi:10.2307/3348768

Fitzpatrick, T., Rosella, L. C., Calzavara, A., Petch, J., Pinto, A. D., Manson, H., . . . Wodchis, W. P. (2015). Looking Beyond Income and Education: Socioeconomic Status Gradients Among Future High-Cost Users of Health Care. *Am J Prev Med, 49*(2), 161-171. doi:10.1016/j.amepre.2015.02.018

Gregori, D., Petrinco, M., Bo, S., Desideri, A., Merletti, F., & Pagano, E. (2011). Regression models for analyzing costs and their determinants in health care: an introductory review. *Int J Qual Health Care, 23*(3), 331-341. doi:10.1093/intqhc/mzr010

Guilcher, S. J., Bronskill, S. E., Guan, J., & Wodchis, W. P. (2016). Who Are the High-Cost Users? A Method for Person-Centred Attribution of Health Care Spending. *PLoS One, 11*(3), e0149179. doi:10.1371/journal.pone.0149179

Hensel, J. M., Taylor, V. H., Fung, K., & Vigod, S. N. (2016). Rates of Mental Illness and Addiction among High-Cost Users of Medical Services in Ontario. *Can J Psychiatry, 61*(6), 358-366. doi:10.1177/0706743716644764

Holtz-Eakin, D. (2005). High-Cost Medicare Beneficiaries Retrieved from http://www.cbo.gov/publication/16487

Lee, J. Y., Muratov, S., Tarride, J. E., & Holbrook, A. M. (2018). Managing High-Cost Healthcare Users: The International Search for Effective Evidence-Supported Strategies. *J Am Geriatr Soc*. doi:10.1111/jgs.15257

Mandrekar JN, & SJ, M. (2004). *An introduction to matching and its application using SAS (Proceedings of the Twenty-ninth Annual SAS Users Group International Conference, 29, 208 'Statistics and Data Analysis')*.

Mondor, L., Walker, K., Bai, Y. Q., & Wodchis, W. P. (2017). Use of hospital-related health care among Health Links enrollees in the Central Ontario health region: a propensity-matched difference-in-differences study. *CMAJ Open, 5*(4), E753-E759. doi:10.9778/cmajo.20170054

Muratov S, Lee J, Holbrook A, Paterson JM, Guertin JR, Mbuagbaw L, . . . TarrideJE. (2018). Regional Variation in Healthcare Spending and Mortality among Senior High-Cost Healthcare Users in Ontario, Canada: a retrospective matched cohort study. *BMC Geriatr*.

Muratov, S., Lee, J., Holbrook, A., Paterson, J. M., Guertin, J. R., Mbuagbaw, L., . . . Tarride, J. E. (2017). Senior high-cost healthcare users' resource utilization and outcomes: a protocol of a retrospective matched cohort study in Canada. *BMJ Open, 7*(12), e018488. doi:10.1136/bmjopen-2017-018488

Nelson, L. (2012). *Lessons from Medicare's Demonstration Projectson Disease Management and Care Coordination*. Retrieved from Washington, D.C.:

Peikes, D., Chen, A., Schore, J., & Brown, R. (2009). Effects of care coordination on hospitalization, quality of care, and health care expenditures among Medicare beneficiaries: 15 randomized trials. *JAMA, 301*(6), 603-618. doi:10.1001/jama.2009.126

Rais, S., Nazerian, A., Ardal, S., Chechulin, Y., Bains, N., & Malikov, K. (2013). High-cost users of Ontario's healthcare services. *Healthc Policy, 9*(1), 44-51.

Reid, R., Evans, R., Barer, M., Sheps, S., Kerluke, K., McGrail, K., . . . Pagliccia, N. (2003). Conspicuous consumption: characterizing high users of physician services in one

Canadian province. *J Health Serv Res Policy, 8*(4), 215-224. doi:10.1258/135581903322403281

Roemer, M. I., & Myers, G. W. (1956). Multiple Admissions to Hospital. *Canadian Journal of Public Health / Revue Canadienne de Sante'e Publique, 47*(11), 469-481.

Roos, N. P., Shapiro, E., & Tate, R. (1989). Does a small minority of elderly account for a majority of health care expenditures? A sixteen-year perspective. *Milbank Q, 67*(3-4), 347-369.

Rosella, L. C., Fitzpatrick, T., Wodchis, W. P., Calzavara, A., Manson, H., & Goel, V. (2014). High-cost health care users in Ontario, Canada: demographic, socio-economic, and health status characteristics. *BMC Health Serv Res, 14*, 532. doi:10.1186/s12913-014-0532-2

Stanton MW, R. M. (2006). *High Concentration of US Health Expenditures*. Retrieved from https://meps.ahrq.gov/data_files/publications/ra19/ra19.pdf

Wammes, J. J. G., van der Wees, P. J., Tanke, M. A. C., Westert, G. P., & Jeurissen, P. P. T. (2018). Systematic review of high-cost patients' characteristics and healthcare utilisation. *BMJ Open, 8*(9), e023113. doi:10.1136/bmjopen-2018-023113

Wodchis, W. P., Austin, P. C., & Henry, D. A. (2016). A 3-year study of high-cost users of health care. *CMAJ, 188*(3), 182-188. doi:10.1503/cmaj.150064

World Health Organization. (2018). Global Health Expenditure Database, 2000-2015. . Retrieved from http://apps.who.int/nha/database/ViewData/Indicators/en

Chapter 2

Open Access Protocol

BMJ Open

Senior high-cost healthcare users' resource utilization and outcomes: a protocol of a retrospective matched cohort study in Canada

Sergei Muratov,[1,2] Justin Lee,[1,3,4,5] Anne Holbrook,[1,4] J Michael Paterson,[6] Jason Robert Guertin,[7,8] Lawrence Mbuagbaw,[1] Tara Gomes,[6,9] Wayne Khuu,[6] Priscila Pequeno,[6] Andrew P Costa,[1,10] Jean-Eric Tarride[1,2,11]

To cite: Muratov S, Lee J, Holbrook A, *et al*. Senior high-cost healthcare users' resource utilization and outcomes: a protocol of a retrospective matched cohort study in Canada. *BMJ Open* 2017;**7**:e018488. doi:10.1136/bmjopen-2017-018488

► Prepublication history and additional material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2017-018488).

Received 3 July 2017
Revised 1 November 2017
Accepted 24 November 2017

For numbered affiliations see end of article.

Correspondence to
Mr. Sergei Muratov; muratos@mcmaster.ca

ABSTRACT

Introduction Senior high-cost users (HCUs) are estimated to represent 60% of all HCUs in Ontario, Canada's most populous province. To improve our understanding of individual and health system characteristics related to senior HCUs, we will examine incident senior HCUs to determine their incremental healthcare utilisation and costs, characteristics of index hospitalisation episodes, mortality and their regional variation across Ontario.

Methods and analysis A retrospective, population-based cohort study using administrative healthcare records will be used. Incident senior HCUs will be defined as Ontarians aged ≥66 years who were in the top 5% of healthcare cost users during fiscal year 2013 but not during fiscal year 2012. Each HCU will be matched to three non-HCUs by age, sex and health planning region. Incremental healthcare use and costs will be determined using the method of recycled predictions. We will apply multivariable logistic regression to determine patient and health service factors associated with index hospitalisation and inhospital mortality during the incident year. The most common causes of admission will be identified and contrasted with the most expensive hospitalised conditions. We will also calculate the ratio of inpatient costs incurred through admissions of ambulatory care sensitive conditions to the total inpatient expenditures. The magnitude of variation in costs and health service utilisation will be established by calculating the extremal quotient, the coefficient of variation and the Gini mean difference for estimates obtained through multilevel regression analyses.

Ethics and dissemination This study has been approved by Hamilton Integrated Research Ethics Board (ID#1715-C). The results of the study will be distributed through peer-reviewed journals. They also will be disseminated at research events in academic settings, national and international conferences as well as with presentations to provincial health authorities.

Strengths and limitations of this study

- ► Focusing on incident senior high-cost users (HCUs) and comparing them with non-HCUs in a longitudinal study allows for scrutiny of the factors that are associated with the transition from non-HCU to HCU and for identification of opportunities of proactive preventive management approaches.
- ► The comparative nature of the study with a matched cohort design reduces bias due to confounding.
- ► This study is subject to the limitations inherent in observational design and the use of health administrative databases.
- ► The study is limited by the period of observation of 1 year before and 1 year after becoming HCU for most of the variables.

INTRODUCTION

Societies worldwide are facing a demographic shift towards a growing proportion of seniors, defined as people aged 65 years and older.[1] In 2015, the proportion of seniors in Canada, for instance, exceeded the proportion of young people (ie, <15 years of age) for the first time in history.[2] Seniors account for 46% of the national public healthcare expenditures in Canada.[3] This proportion is likely to increase due to the continued ageing of the population, therefore putting additional pressure on the government's resource allocation decisions in the coming years. The high-cost users (HCUs) of health services,[4 5] commonly defined as individuals in the highest 5% of total expenditures, are often seniors. Senior HCUs are estimated to represent 60% of all HCUs in Ontario, Canada's most populous province.[4] Consistent with findings from other jurisdictions,[6 7] a recent Ontario study indicated that 5% of senior HCUs consume 44% of the total measured public healthcare expenditures by the seniors in the province.[8]

A number of demographic and clinical characteristics of the senior HCUs have been described internationally and in Canada: high level of comorbidities, functional impairment and poor social supports at home.[8–10] However, many individual and health system characteristics related to senior HCUs are still poorly understood, particularly in the context of their subpopulations. As such, many disease management programmes as well as research efforts focus on persistent HCUs, that is, those who retain their HCU status in subsequent years.[8 11 12] This practice ignores the fact that 'new', or incident, HCUs have historically accounted for more than 50% of all the cases annually, including those among senior patients.[8 13] Incident senior HCUs may have different characteristics than prevalent HCUs, and more focus on incident HCUs will allow for scrutiny of the factors that influence the transition from non-HCU to HCU.

Filling gaps in our understanding of this HCU subgroup is especially important at a time when policy makers internationally are targeting interventions for senior HCUs such as complex case management and care coordination models.[8 12 14 15] To inform policy making in identification of opportunities to prevent transition to the HCU status or to improve existing programmes, a closer inquiry is required into the incident senior HCUs in terms of their incremental healthcare utilisation and costs, characteristics of their hospitalisation episodes, including the economic impact of individual conditions, and regional variation in main outcomes.

Incremental costs among incident HCUs

The magnitude of incremental healthcare utilisation and costs attributable to becoming a HCU is unknown. HCU research in Canada and elsewhere has been conducted predominantly on prevalent HCU cohorts using cross-sectional designs.[4 7 8 16–18] These studies provide valuable information on comparisons, for example, of the 1 year costs of HCUs compared with non-HCUs. However, these methods do not explore the change in outcomes associated with becoming a new HCU beyond secular trends in outcomes over time, thus missing the contribution of HCU status. In addition, no study to our knowledge has compared the characteristics, costs and outcomes of incident HCUs to a matched cohort of non-HCUs, which would provide a more detailed assessment of the distinguishing features of HCU status. Finally, HCU-related research with a system-wide approach is still limited[4 8] as studies have largely focused on acute care (eg, hospitalisations, emergency care and physicians) and have left out other important care categories such as long-term care, rehabilitation and medications. Recently, a population-based study conducted in Ontario, Canada, took a 1 year look at the cost distribution across a wider range of health sectors among HCUs, including seniors.[8] Although it was applied to prevalent HCUs and was not intended to provide a detailed characterisation of the study population and a comparison with non-HCUs, we will be building on their work by using the same cost algorithm.

Analysis of hospitalisation episodes among senior incident HCUs compared with non-HCUs

The majority (>90% in some studies) of senior HCUs have at least one hospital admission in the year they reach HCU status.[13] Considering that hospitalisation costs among HCUs may account for almost two-thirds of direct medical costs,[4] it is important to better understand the characteristics associated with hospitalisations among incident HCUs. To date, much of the literature on risk factors and interventions to prevent hospitalisation has focused on hospital readmissions.[19–22] However, as opposed to younger adults in whom hospitalisations often occur due to a sudden event (eg, trauma) that often resolves without serious permanent cost or care implications,[23] readmissions in senior patients, especially HCUs, may signal a deterioration in health status and mark a point where management interventions are less likely to be effective in preventing recurrent hospitalisations.[12] Therefore, focusing on the index hospitalisations associated with becoming an incident senior HCU (ie, the first admission in the fiscal year when the patient reaches the HCU status) with the goal to reduce or divert them may be a more appropriate target for policy development. Since this subject has received little attention,[24] more information is needed on the index hospitalisation, including the patient demographic and clinical attributes (eg, whether the patient is admitted for a newly diagnosed condition or a condition that he or she has received care in preceding years), outpatient care that was provided prior to the admission (eg, type of home care visits) and the environment within which the care is received (eg, primary care model).

Determining the most expensive conditions by inpatient costs and identifying patient attributes associated with them is also of great interest to health planners and administrators as a potential target for cost containment strategies. In this respect, the contribution of ambulatory care sensitive conditions (ACSC) to HCU requires clarification. ACSC-related hospital admissions, that is, those that are theorised to be reducible with high-quality primary care,[25 26] have been long used as an indicator of access to primary care at the population level.[27–29] In Canada, several chronic ACSCs are on a national list of indicators of health system performance reported by health authorities.[30] However, the economic impact of ACSC admissions among HCUs is unclear. A recent US study revealed that no more than 10% of hospitalisation costs among the top decile of Medicare HCUs were ACSC related.[31] The authors commented that if the financial impact of ACSC is low and resource consumption is a target for intervention, it may be worthwhile to shift prevention efforts to other conditions that are financially more burdensome. The only Canadian study of this issue reported that 6% of hospital encounters among HCUs were considered ambulatory sensitive. This study however was different from the US study in that it defined the top 5th percentile as HCUs (versus 10th), investigated a broader population (children and adults up to 75 years of age) admitted to a single tertiary hospital in Ottawa, Ontario, and estimated the ACSC costs focusing on a shorter list of chronic conditions.[32] As such, we do not know if these results are generalisable to all hospitalisations in Ontario and to the senior HCUs. None of these studies have focused on incident HCUs in which the economic impact from ACSCs may be different compared with persistent HCUs or on the relative contribution of ACSCs on the index hospitalisations during the incident year.

Regional variation in health services use, costs and mortality among incident senior HCUs

Finally, studying regional variation is needed to understand equality in service provision and identify areas for interventions. Evidence on geographic variation in healthcare utilisation, costs and mortality among senior HCUs is scarce.[4 33] In Canada's general population, variation in health service use (eg, hospital admission rates, surgical procedures or consumption of medications), both at provincial level and when compared with other countries, can be substantial.[34–37 37] This observation however may be misleading as assessments of variation are commonly adjusted for age and sex only[36–39] despite numerous reports revealing the impact of sociodemographic or healthcare supply factors on this variation.[35 40–42] However, healthcare spending may show a lower level of variability. For example, a recent study conducted in British Columbia, Canada, reported a coefficient of variation (CV) for total healthcare spending of 8.6 (4.9 on adjustment).[40] This is lower compared with the US and the UK that reported CVs of approximately 12 and 10, respectively.[43] It is unclear how all these findings relate to senior HCUs in the context of Ontario. Also, assessment of regional variation in individual cost categories has not been reported.

Furthermore, geographical units should reflect actual patterns of services use. In Ontario, delivery of care is organised by health planning regions. These regions were originally established to reflect local patterns of clinical decision making and use of services. However, inter-region migration to receive health services is common. The proportion of expenses incurred for acute care provided in health facilities outside the region of residence ranged from 3% to 49% depending on the region.[33] The impact of such migration on regional variation in healthcare use and spending among HCUs has received little attention in the literature, although potential budget planning implications for health planning regions can be sizeable due to the high costs associated with HCUs.

Here, we propose to answer three inter-related research questions:

1. What is the 1-year incremental healthcare utilisation and direct financial impact on public payers of becoming an incident HCU among seniors in Ontario? Hypothesis: the greatest incremental value in utilisation and expenditures will be attributable to hospitalisation episodes followed by physician costs.
2. What are the characteristics of hospital admissions and associated costs in senior incident HCUs compared with non-HCUs in Ontario? Hypotheses: (A) causes of hospitalisation as well as individual and care factors associated with an index hospitalisation for senior HCUs differ from those of non-HCUs; and (B) the contribution of ACSCs will be high (proportion >10% of the total hospitalisation costs) in senior HCUs and significantly higher than among non-HCUs.
3. What is the extent of regional (health planning level) variation in healthcare utilisation, costs and mortality among senior incident HCUs compared with non-HCUs in Ontario? Hypothesis: regional variation in utilisation, sector-specific costs and mortality measured by CV will be significantly higher in the HCU cohort than non-HCUs.

METHODS AND ANALYSIS

Study design

The proposed study is a retrospective population-based matched cohort study using linked administrative health data. Registration number is NCT02815930 (clinicaltrials.gov).

Setting

Ontario is the most populous province in Canada, with almost 14 million residents, representing about 40% of the Canadian population.[44] It is divided into 14 Local Health Integration Networks (LHIN) that are responsible for local healthcare planning and delivery.[45] The Ontario Ministry of Health and Long-Term Care (MOHLTC), using general taxation revenues (80% provincial and 20% federal transfer), pays for approximately 70% of healthcare provided in the province. This includes 90%–100% funding of hospital care, physician costs, public health and prescription drugs for seniors,[3] while contributions to other services (eg, long-term care facilities) are less.

Study cohorts

The study population is senior HCUs with annual total healthcare expenditures within the top 5% threshold of all Ontarians in the fiscal year of 2013 (ie, incident year), who were not in the top 5% in the preceding year. Total healthcare expenditures will be calculated using the Institute of Clinical Evaluative Sciences (ICES) person-level health utilisation costing algorithms.[46] ICES is an independent, non-profit research corporation funded by the MOHLTC (www.ices.on.ca).

To reduce bias due to confounding, the incident HCU cohort will be matched with non-HCU in a ratio of 1:3 according to age at cohort entry (±1 month), sex and LHIN of patient residence. Health services utilisation and costs will be captured from 1 April 2013 to 31 March 2014.

Data set

The patient level dataset will be created using 15 health administrative databases housed at ICES. These databases contain publicly funded administrative health service records for the Ontario population eligible for health coverage. These databases are linked using encrypted patient-specific identifiers. Online supplementary appendix 1 presents a description of databases that will be used to create the dataset.

Variables

The dataset will include a number of variables related to patient sociodemographic characteristics, healthcare use and patient outcomes that are briefly described below (see online supplementary appendix 2 for more detail on key variables).

Patient characteristics include age, sex, geographic location, income (in quintiles), immigration status and comorbidity. Geographical location of residence (urban/suburban/rural) is based on the Rural Index of Ontario (RIO) and LHIN.[47] Multimorbidity is captured by means of John Hopkins Expanded Diagnosis Clusters (EDCs). EDCs are derived from Johns Hopkins Adjusted Clinical Groups (www.hopkinsacg.org),[48] which are used to organise the codes of the International Statistical Classification of Diseases and Related Health Problems, the 10th revision, Canadian version (ICD10-CA)[49] into 282 clinically similar clusters. EDCs will be based on 3 years of hospitalisation and ambulatory data prior to index date.

Care characteristics include the primary care provider payment model. The providers are categorised by several main primary care patient enrolment models: fee for service (FFS), enhanced FFS, Family Health Team (FHT), capitation and none. Under enhanced FFS model, provider's compensation is based on FFS billing with enhanced FFS components and incentives for the provision of services for specific patient needs. FHT models consists of two options: the primarily capitation-based Family Health Network (FHN) and the capitation or salaried-based Family Health Organization (FHO). If the patient is affiliated with either FHN or FHO but not matched to FHT, then the patient is placed with the capitation category. The none category refers to patients for whom no primary care provider was identified (ie, they were not enrolled with a provider through a patient enrolment programme, and they were not virtually rostered based on claims because they did not have any billing claims with primary care fee codes).

Resource utilisation variables include the number of hospitalisations, emergency department (ED) visits, physician encounters, publicly funded home care visits and long-term care. Home care visits are categorised by type of services provided such as nursing, personal support or allied health. For each hospitalisation, the following information is derived: admission type (urgent or elective), length of stay, the type of institution the patient has been transferred from, alternate level of care (ALC) status, discharge destination, date of death while in hospital, whether the hospitalisation happened within the LHIN of residence and hospitalisation costs. All healthcare expenditures are derived using the ICES costing algorithm for each cost category.

Study primary outcomes

1. One-year incremental healthcare utilisation (rate per 10 000 of study population for hospital admissions, ED, physician and home care visits) and costs (mean) attributable to becoming an HCU at the provincial level (research question 1).
2. Determination of patient and care factors associated with (A) index hospitalisation (OR) and (B) its in-hospital mortality (OR) among HCUs and non-HCUs during the incident year (research question 2).
3. Proportion (%) of ACSC-related hospitalisation costs to annual total inpatient costs during the incident year at the provincial level for the HCU and non-HCU cohorts (research question 2).
4. Patterns of variation in healthcare utilisation, mortality and costs across LHINs in HCUs compared with non-HCUs during the incident year (research question 3).

ANALYSIS PLAN

The two matched cohorts (HCUs and non-HCUs) will be described using descriptive statistics. In addition to standardised differences[50] to compare the baseline characteristics of the two cohorts, regression methods will be used to adjust for important residual differences between the cohorts that remain after matching. Each subsection below presents more detail on handling confounding. Data preparation before running regression analyses will include identifying colinearity between covariates. Goodness-of-fit statistics will be used to evaluate models and guide model selection. A level of $\alpha < 0.05$ will be applied to indicate statistical significance.

Regression models for cost and count data including two-part models to deal with the potential over-representation of zeros in the data will be used to analyse the data. For example, we expect that many members in the non-HCU cohort may have no encounters with the health system (ie, no hospital admission, physician visits or visits to ED). Ignoring the fact that the data are not normally distributed or using only the portion of the data with the values greater than zero can lead to biased estimates.[51] The following provides more information on the analysis plan for each of the three research questions.

Research question 1

To estimate the incremental healthcare utilisation and costs attributable to becoming an HCU, longitudinal data analysis will be employed.[52] The HCU dataset containing repeated measures on the same subject (ie, 1 year prevalues and postvalues) is an example of longitudinal data. Incremental values of the outcome variables (ie, costs, physician encounters and so on) represent the difference between the two cohorts over time. An estimate of incremental values will be generated using the method of recycled predictions.[53–56] First, coefficients are obtained from a model regressing the postvalues of an outcome on the HCU status, prevalues of the outcome and other covariates as needed. Then, using the calculated coefficients, predicted outcome values are estimated assuming everyone is an HCU and re-estimated assuming every subject is a non-HCU. The difference between the two averaged predictions yields the incremental value. CIs of the incremental values will be obtained with the percentile method (ie, creating a bootstrap distribution and assigning the 95% lower bound CI to the 2.5th percentile and the 95% upper bound CI to the 97.5th percentile).[56] The method will be applied to analyse incremental changes in each type of costs and healthcare utilisation.

Muratov S, *et al*. *BMJ Open* 2017;**7**:e018488. doi:10.1136/bmjopen-2017-018488

This approach will allow us to account for correlation between the prevalues and postvalues, to adjust for residual confounding by including demographic (ie, income) and health status (ie, comorbidities) variables in the model and, when needed, to properly manage excessive zero values by developing two-part models. Alternative models may also be explored to accommodate the data specifics (eg, mixed models with random effects).

Research question 2

To describe and compare characteristics of the index hospitalisation among senior HCUs versus non-HCUs during the incident year (fiscal year 2013), we will define an index hospitalisation as the first hospitalisation in the incident year among subjects without admissions of any type in the preceding year (fiscal year 2012). We will provide descriptive statistics on hospitalisations by the type of admission (frequency of urgent vs elective), by the total length of stay (mean), including the ALC status and the number of ALC days (mean), by discharge destination (frequency) and inhospital mortality. Using major ICD10-CA diagnosis codes responsible for resource use (abbreviated as MRDX), we will identify the most common clinical causes of admissions and contrast the list with a list of most expensive hospitalised conditions for both cohorts to distinguish common diagnoses from diagnoses that drive inpatient spending. To determine patient and care factors associated with index hospitalisation and its inhospital mortality (dependent variables) during the incident year, we will develop predictive models using multivariable logistic regression based on a list of predetermined demographic, clinical and care factors (online supplementary appendix 3).

To investigate the proportion of ACSC-associated hospitalisation costs, we will identify patients admitted for ACSCs and calculate for the HCU and the non-HCU cohorts the ratio of inpatient costs incurred through ACSC admissions to the total inpatient expenditures. Our ACSC list will be based on the list originally developed by the Agency for Healthcare Research and Quality (AHRQ).[29] Chronic conditions on the list (eg, hypertension, diabetes and so on) will be identified using the Canadian Institute of Health Information (CIHI) ACSC algorithm,[27] which is based on the AHRQ original list adapted to Canada. The algorithm for three other conditions considered acute (eg, bacterial pneumonia, dehydration and urinary tract infections) and not included in the CIHI algorithm of chronic conditions will be derived by directly converting the original ICD-10-CM codes of the AHRQ original list into ICD-10-CA. Online supplementary appendix 4 provides more detail on the algorithms.

Consistent with the approach to ACSC identification that was previously used by researchers,[27 32 57] ACSC-related hospitalisations can be identified using the most responsible diagnosis at discharge. However, using the most responsible diagnosis that accounts for the largest portion of consumed resources during the hospitalisation may not be able to accurately capture all ACSC-associated admission costs. Applying an ACSC definition to preadmission diagnoses that also add to the use of resources[57] would help clarify the economic impact of ACSCs among incident senior HCUs. Therefore, ACSC diagnosis codes will be included when they are accompanied by diagnosis types of either 'M' (MRDX) or '1' (preadmission diagnosis) without an accompanying '2' (postadmission diagnosis).[57] Of note, no studies have compared these two approaches before to identify ACSC related costs. The ACSC definition will be applied to patients in the incident year. Transfers will be excluded from the definition of hospitalisation episode.

Sensitivity analysis will be conducted to assess the impact of several factors on hospitalisation costs. Analysis will be repeated for three age subgroups: those age 66–74 years, 75–84 years and 85 years and older. As sepsis cases (reportedly, one of the costliest among hospitalised conditions) may go under-reported when using MRDX codes alone,[58] the case-finding algorithm to capture these cases will include preadmission and postadmission codes that are not MRDX. We will also apply the ACSC algorithm excluding non-emergent hospitalisations and readmissions. The ACSC-related costs will be compared with non-ACSC inpatient costs in both cohorts.

Research question 3

To assess regional differences among senior HCUs compared with non-HCUs, we will focus on the incident year and use several approaches. First, we will make a cross-sectional comparison of patients' clinical, demographic and care characteristics for each LHIN contrasting the two cohorts. Within each LIHN, urban, sub-urban and rural residence characteristics by RIO will be taken into account. Crude HCU rate per LHIN seniors will be derived to identify areas of high and low HCU incidence.

Second, we will estimate regional variation in total healthcare spending and health services utilisation and contrast these values between the two cohorts.[59] Regression models with LHIN-level fixed effects will be developed using the following as dependent variables: total and sector healthcare expenditures, count data (ie, hospital admission, emergency visits, physician encounters and home care visits) and mortality. The crude values will be then adjusted to remove the influence of comorbidity, demographic and care factors or RIO status.

The magnitude of variation will be quantified using the extremal quotient (EQ), the CV and the Gini mean difference (GMD). The EQ is the ratio of the highest LHIN parameter to the lowest. The CV is the ratio of the SD to the mean among the LHINs: the higher the CV, the greater the dispersion. Both are widely used nationally and internationally.[37 38] The GMD has been commonly used in economics and social sciences to measure inequality and variability and is gaining popularity in health sciences.[60] It calculates the extent to which the distribution of a parameter (eg, total costs) among individuals across LHINs deviates from an exactly equal distribution.

Third, we will describe inter-LHIN migration patterns to receive acute hospital care and assess its impact on regional variation in total health spending for both cohorts. We will rerun the total healthcare spending regression model described above with the proportion of residents of a LHIN admitted outside the LHIN taken out of the analysis. The EQ, the CV and the GMD will be used to compare the models and the cohorts.

Significance and policy implications of study results

This study will generate new knowledge that will assist Canadian healthcare administrators, clinicians, citizens and patients to guide health policy and programme development around senior HCUs. The analysis of incremental healthcare utilisation and costs will provide a description of the true utilisation and economic impact associated with the incident HCU status. By separating index hospitalisations, the analysis of hospitalisation patterns in the incident cohort of senior HCUs compared with matched non-HCUs will help identify potential interventions to prevent or divert hospitalisation episodes for high-risk groups. Exploring the contribution of disease-specific hospitalisation costs towards the total inpatient spending will help determine the potential value expanding care models that target ACSCs and identify opportunities of fund reallocation to hospitalisations types that are more contributory and more amenable to change. Furthermore, by defining regional variation in healthcare services and spending among senior HCUs, we will inform the value of potential benchmarking and regional practice comparisons in HCU management. Finally, since other jurisdictions in developed countries have comparable health systems and are faced with similar HCU challenges, our methods and findings may inform local considerations for HCU prevention and management.

Exploratory analysis

Explanatory analyses may be conducted to explore study-specific populations, cost thresholds to determine HCU status (1% vs 5%) or any other relevant factors. ICES-derived cohorts will be used to facilitate the analysis. These cohorts were created by identifying patients with specific diseases (eg, chronic obstructive pulmonary disease, congestive heart failure and diabetes) using validated case-finding algorithms.[61 62]

Ethics and dissemination

The results of the study will be distributed widely through peer-reviewed journals. They also will be disseminated at research events in academic settings, national and international conferences as well as with presentations to the MOHLTC and LHIN administration.

Author affiliations
[1]Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada
[2]Programs for Assessment of Technology in Health (PATH), The Research Institute of St. Joe's Hamilton, St. Joseph's Healthcare, Hamilton, Ontario, Canada
[3]Division of Geriatric Medicine, Department of Medicine, McMaster University, Hamilton, Ontario, Canada
[4]Division of Clinical Pharmacology and Toxicology, Department of Medicine, McMaster University, Hamilton, Ontario, Canada
[5]Geriatric Education and Research in Aging Sciences Centre, Hamilton Health Sciences, Hamilton, Ontario, Canada
[6]Institute for Clinical Evaluative Sciences (ICES), Toronto, Ontario, Canada
[7]Département de médecine sociale et préventive, Faculté de Médecine, Université Laval, Quebec City, Quebec, Canada
[8]Centre de recherche du CHU de Québec, Université Laval, Axe Santé des Populations et Pratiques Optimales en Santé, Quebec City, Quebec, Canada
[9]Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Ontario, Canada
[10]Big Data and Geriatric Models of Care Cluster, Department of Medicine, McMaster University, Hamilton, Ontario, Canada
[11]Center for Health Economics and Policy Analysis (CHEPA), McMaster University, Hamilton, Ontario, Canada

Contributors SM, J-ET, AH, JL, JMP, TG and JRG conceptualised the study. All authors have contributed to its design. JMP, WK, PP and TG were instrumental in creating datasets. SM prepared the initial draft of the manuscript and revised it based on co-authors' feedback: J-ET, AH, JL, JMP, TG, JRG, LM, APC, WK and PP provided comments to the initial draft, further revisions and read and approved the final manuscript. The responsibility of study implementation lies with the principle investigator (SM) that is supported and supervised primarily by J-ET.

Funding This work is supported by personnel funding and in-kind analyst and epidemiologist support from the Ontario Drug Policy Research Network (ODPRN) and personnel awards from the Canadian Institutes of Health Research (CIHR) Drug Safety and Effectiveness Cross-Disciplinary Training (DSECT) Program, the Program For Assessment of Technology in Health (PATH) and an Ontario Graduate Scholarship (OGS). The ODPRN is funded by grants from the Ontario Ministry of Health and Long-Term Care (MOHLTC) and Ontario Strategy for Patient-Orientated Research (SPOR) Support Unit, which is supported by the Canadian Institutes of Health Research and the Province of Ontario. The opinions, results and conclusions reported in this article are those of the authors and are independent from the funding sources. No endorsement by the Ontario MOHLTC is intended or should be inferred.

Competing interests None declared.

Ethics approval This study has been approved by Hamilton Integrated Research Ethics Board (ID#1715-C).

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1. *World population ageing 2013*: United Nations, Department of Economic and Social Affairs, Population Division, 2013.
2. Institute for Research on Public Policy. 2015. Designing a national seniors strategy for Canada, IRPP task force on aging: Institute for Research on Public Policy.
3. Canadian Institute for Health Information. 2016. National health expenditure trends, 1975 to 2016. Ottawa: Canadian Institute for Health Information.
4. Rais S, Nazerian A, Ardal S, *et al*. High-cost users of Ontario's healthcare services. *Healthc Policy* 2013;9:44–51.
5. Rosella LC, Fitzpatrick T, Wodchis WP, *et al*. High-cost health care users in Ontario, Canada: demographic, socio-economic, and health status characteristics. *BMC Health Serv Res* 2014;14:532.
6. Central Midlands CSU NHS. The total cost of care for older people in Solihull - an analysis of combined NHS and social care data. 2014 https://solihullccg.nhs.uk/publications/1245-bcf-cost-of-care/file (accessed 20 May 2017).
7. Stanton MW RM. *High concentration of US health expenditures*: Research in Action, Agency for Healthcare Research and Quality, 2006.
8. Wodchis WP, Austin PC, Henry DA. A 3-year study of high-cost users of health care. *CMAJ* 2016;188:182–8.
9. Sinha SK. Why the elderly could bankrupt Canada and how demographic imperatives will force the redesign of acute care service delivery. *Healthc Pap* 2011;11:46–51.

10. Holtz-Eakin D. High-cost medicare beneficiaries 2005. 2005 http://www.cbo.gov/publication/16487 (accessed 25 Apr 2017).
11. Nelson L. *Lessons from medicare's demonstration projectson disease management and care coordination*. Washington, DC: Health and Human Resources Division Congressional Budget Office, 2012.
12. Peikes D, Chen A, Schore J, *et al*. Effects of care coordination on hospitalization, quality of care, and health care expenditures among Medicare beneficiaries: 15 randomized trials. *JAMA* 2009;301:603–18.
13. Roos NP, Shapiro E, Tate R. Does a small minority of elderly account for a majority of health care expenditures? A sixteen-year perspective. *Milbank Q* 1989;67:347–69.
14. Blumenthal D, Chernof B, Fulmer T, *et al*. Caring for high-need, high-cost patients - an urgent priority. *N Engl J Med* 2016;375:909–11.
15. Stokes J, Panagioti M, Alam R, *et al*. Effectiveness of case management for 'At Risk' patients in primary care: a systematic review and meta-analysis. *PLoS One* 2015;10:e0132340.
16. Fitzpatrick T, Rosella LC, Calzavara A, *et al*. Looking beyond income and education: socioeconomic status gradients among future high-cost users of health care. *Am J Prev Med* 2015;49:161–71.
17. Reid R, Evans R, Barer M, *et al*. Conspicuous consumption: characterizing high users of physician services in one Canadian province. *J Health Serv Res Policy* 2003;8:215–24.
18. Guilcher SJ, Bronskill SE, Guan J, *et al*. Who are the high-cost users? A method for person-centred attribution of health care spending. *PLoS One* 2016;11:e0149179.
19. Dattalo M, Nothelle S, Chapman EN. Targeting enhanced services toward high-cost, high-need medicare patients. 2016:19–30.
20. Iloabuchi TC, Mi D, Tu W, *et al*. Risk factors for early hospital readmission in low-income elderly adults. *J Am Geriatr Soc* 2014;62:489–94.
21. Goncalves-Bradley DC, Lannin NA, Clemson LM, *et al*. Discharge planning from hospital. *The Cochrane database of systematic reviews* 2016;1:Cd000313.
22. Kellogg FR, Brickner PW, Conley L, *et al*. Controlling hospital readmission of elderly persons living at home: a risk factor analysis. *Home Health Care Serv Q* 1991;12:5–16.
23. White Paper, Health Care Transformation Task Force. Health care transformation task force. 2015 http://hcttf.org/resources-tools-archive/2015/5/14/whitepaper (accessed 10 Mar 2017).
24. Wallace E, Stuart E, Vaughan N, *et al*. Risk prediction models to predict emergency hospital admission in community-dwelling adults: a systematic review. *Med Care* 2014;52:751–65.
25. Ministry of Health and Long Term Care. Health system information management & investment division. Health analytics branch. http://www.health.gov.on.ca/en/pro/programs/ris/docs/ambulatory_care_sensitive_conditions.pdf (accessed 20 Nov 2016).
26. Billings J, Zeitel L, Lukomnik J, *et al*. Impact of socioeconomic status on hospital use in New York City. *Health Aff* 1993;12:162–73.
27. Canadian Institute for Health Information. Ambulatory care sensitive conditions, 2016. http://indicatorlibrary.cihi.ca/display/HSPIL/Ambulatory+Care+Sensitive+Conditions
28. Longman JM, Passey ME, Ewald DP, *et al*. Admissions for chronic ambulatory care sensitive conditions - a useful measure of potentially preventable admission? *BMC Health Serv Res* 2015;15:472.
29. Agency for Healthcare Research and Quality. AHRQ Quality Indicators—prevention quality indicators technical specifications updates. Version 6.0 (ICD 10 http://www.qualityindicators.ahrq.gov/Modules/PQI_TechSpec_ICD10_v60.aspx 2016.
30. Ontario South West Local Health Integration Network. Report on performance: technical specifications. 2017 http://www.southwestlhin.on.ca/accountability/Performance.aspx#Big%20Dot%20and%20Priority%20Summaries
31. Joynt KE, Gawande AA, Orav EJ, *et al*. Contribution of preventable acute care spending to total spending for high-cost Medicare patients. *JAMA* 2013;309:2572–8.
32. Ronksley PE, Kobewka DM, McKay JA, *et al*. Clinical characteristics and preventable acute care spending among a high cost inpatient population. *BMC Health Serv Res* 2016;16:165.
33. Health Analytics Branch, HSIMI. High cost users for local health integrated networks. 2013 http://southwestlhin.on.ca/~/media/sites/sw/uploadedfiles/Public_Community/Current_Initiatives/Health_Links/Describing%20High%20Users_HAB_overview_September%202013%20
34. Corallo AN, Croxford R, Goodman DC, *et al*. A systematic review of medical practice variation in OECD countries. *Health Policy* 2014;114:5–14.
35. Hogan DB, Maxwell CJ, Fung TS, *et al*. Regional variation in the use of medications by older Canadians--a persistent and incompletely understood phenomena. *Pharmacoepidemiol Drug Saf* 2003;12:575–82.
36. Feinberg AE, Porter J, Saskin R, *et al*. Regional variation in the use of surgery in Ontario. *CMAJ Open* 2015;3:E310–E316.
37. Geographic Variations in Health Care. Focus on health- OECD health policy studies. 2014 https://www.oecd.org/els/health-systems/FOCUS-on-Geographic-Variations-in-Health-Care.pdf (accessed 18 May 2017).
38. Feasby TE, Quan H, Ghali WA. Geographic variation in the rate of carotid endarterectomy in Canada. *Stroke* 2001;32:2417–22.
39. Kim AM, Park JH, Kang S, *et al*. The effect of geographic units of analysis on measuring geographic variation in medical services utilization. *J Prev Med Public Health* 2016;49:230–9.
40. Lavergne MR, Barer M, Law MR, *et al*. Examining regional variation in health care spending in British Columbia, Canada. *Health Policy* 2016;120:739–48.
41. Kephart GAY, Atherton F, Burge F, *et al*. *Small area variation in rates of high-cost healthcare use across Nova Scotia*. Halifax, Nova Scotia: Maritime SPOR SUPPORT Unit, 2016.
42. Morgan SG, Cunningham CM, Hanley GE. Individual and contextual determinants of regional variation in prescription drug use: an analysis of administrative data from British Columbia. *PLoS One* 2010;5:e15883.
43. Congressional Budget Office, Congress of The United States. Geographic variation in health care spending. 2008 https://www.cbo.gov/sites/default/files/cbofiles/ftpdocs/89xx/doc8972/02-15-geoghealth.pdf (accessed 8 Jun 2017).
44. Statistics Canada. Population by year, by province and territory. 2016 http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/demo02a-eng.htm (accessed 26 Apr 2017).
45. Office of the Audit or General of Ontario. 2015. Annual report 2015: Office of the Audit or General of Ontario.
46. Wodchis WP, Bushmeneva K, Nikitovic M, *et al*. *Guidelines on person-level costing using administrative databases in Ontario*1. Working Paper Series 2013.
47. Kralj B. *Measuring 'rurality' for purposes of health-care planning: an empirical measure for Ontario*: Ontario Medical Review, 2000.
48. *The Johns Hopkins ACG® system version 11.0 technical reference guide*: Department of Health Policy and Management, Johns Hopkins University, Bloomberg School of Public Health, 2014.
49. Canadian Institute for Health Information. *ICD-10-CA (International statistical classification of diseases and related health problems, 10th Revision, Canada)*. (accessed 25 May 2017).
50. Austin PC. Using the standardized difference to compare the prevalence of a binary variable between two groups in observational research. *Commun Stat Simul Comput* 2009;38:1228–34.
51. Tooze JA, Grunwald GK, Jones RH. Analysis of repeated measures data with clumping at zero. *Stat Methods Med Res* 2002;11:341–55.
52. Diggle PJ HP, Liang K-Y, Zeger SL. *Analysis of longitudinal data*. 2nd edn. Clarendon: Oxford University Press Inc, 2002.
53. Basu A, Arondekar BV, Rathouz PJ. Scale of interest versus scale of estimation: comparing alternative estimators for the incremental costs of a comorbidity. *Health Econ* 2006;15:1091–107.
54. Chang C, Lee SM, Choi BW, *et al*. Costs attributable to overweight and obesity in working asthma patients in the United States. *Yonsei Med J* 2017;58:187–94.
55. Lange A, Zeidler J, Braun S. One-year disease-related health care costs of incident vertebral fractures in osteoporotic patients. *Osteoporos Int* 2014;25:2435–43.
56. Mannino DM, Higuchi K, Yu TC, *et al*. Economic Burden of COPD in the presence of comorbidities. *Chest* 2015;148:138–50.
57. Walker JD, Teare GF, Hogan DB, *et al*. Identifying potentially avoidable hospital admissions from canadian long-term care facilities. *Med Care* 2009;47:250–4.
58. Rhee C, Dantes R, Epstein L, *et al*. Incidence and trends of sepsis in US hospitals using clinical vs claims data, 2009-2014. *JAMA* 2017;318:1241–9.
59. Austin P, Merlo J. *Intermediate and advanced topics in multilevel logistic regression analysis*, 2017.
60. Gadrich T, Bashkansky E, Zitikis R. Assessing variation: a unifying approach for all scales of measurement. *Qual Quant* 2015;49:1145–67.
61. Gershon AS, Wang C, Guan J, *et al*. Identifying individuals with physcian diagnosed COPD in health administrative databases. *COPD* 2009;6:388–94.
62. Schultz SE, Rothwell DM, Chen Z, *et al*. Identifying cases of congestive heart failure from administrative data: a validation study using primary care patient records. *Chronic Dis Inj Can* 2013;33:160–6.

Appendix 1: Description of ICES databases

NAME OF DATABASE	DATABASE CONTENT
Canadian Institute for Health Information–Discharge Abstract Database (CIHI-DAD)	Patient-level demographic, diagnostic, procedural and treatment information on all acute care hospitalizations
CIHI—National Ambulatory Care Reporting System (CIHI-NACRS)	Patient-level demographic, diagnostic, procedural and treatment information for all hospital-based and community-based ambulatory care, including outpatient and community-based clinics and emergency departments
CIHI-National Rehabilitation Reporting System (NRS)	Patient-level demographic, diagnostic, procedural and treatment information from participating adult inpatient rehabilitation facilities and programs
CIHI-Same Day Surgery (CIHI-SDS)	Patient-level demographic, diagnostic, procedural and treatment information on all day surgeries
Citizenship and Immigration Canada (CIC) Database	Landing records for permanent legal immigrants to Ontario
Client Agency Program Enrolment (CAPE)	Information regarding enrollment/rostering of individuals with primary care practitioners, teams and networks
ICES Physician Database (IPDB)	Characteristics of physicians and surgeons licenced to practice in Ontario
ICES-derived cohorts	Validated cohorts of individuals with specific diseases and conditions. These include: Congestive Heart Failure (CHF) database; Chronic Obstructive Pulmonary Disease (COPD) database; Ontario Crohn’s and Colitis Cohort Database (OCCD); Ontario Diabetes Database (ODD); Ontario Myocardial Infarction Database (OMID); and the Ontario Rheumatoid Arthritis Database (ORAD)
Ontario Continuing Care Reporting System (CCRS)	Demographic, clinical, functional and resource utilization information on individuals receiving hospital-based complex continuing care services
Ontario Drug Benefit (ODB)	Records of dispensed outpatient prescriptions paid for by the provincial government
Ontario Health Insurance Plan database (OHIP)	Claims for physician services paid for by the provincial government
Ontario Home Care Database (HCD)	Patient-level demographic, diagnostic, procedural and treatment information on all home care visits
Ontario Mental Health Reporting System (OMHRS)	Patient-level demographic, diagnostic, procedural and treatment information on all adult inpatient mental health visits
Ontario Registered Persons Database (RPDB)	Demographic, place of residence and vital status information for all persons eligible to receive insured heath services in the province

Appendix 2: Key variables and sources of data

Key variables	**Description**	**Type**	**Time period (PRE=1, POST=2)**	**Data source**
Patient and care characteristics				
age_	Age in years	continuous	1	RPDB
sex_	Sex; female or male	categorical	1	RPDB
rio2008_	Rurality Index for Ontario; on a scale of 0 to 100 with 100 being most rural	continuous	1	RPDB
lhin_	LHINs: 1 to 14	categorical	1	RPDB
income_	Income quintiles	categorical	1	RPDB
recent_immigration_	Whether immigrated in the past 15 years	categorical	1	CIC
primarycaregrp_	Primary care model	categorical	1	CAPE
geriatrician_	Whether visited a geriatrician	categorical	1	OHIP
Health status/comorbidity				
n_edc	John Hopkins Expanded Diagnosis Clusters (EDCs) are based on 3 years of hospitalization and ambulatory data	continuous	1	DAD, NACRS, OHIP
ices_cohort_	Cohorts of individuals with the following conditions separately: CHF, COPD, Inflammatory Bowel Disease (Crohn's and Colitis), diabetes, myocardial infarction, or rheumatoid arthritis	categorical	1	CHF, COPD, OCCD, ODD, OMID, ORAD
dth365d_	Mortality at the end of FE2013	categorical	2	RPDB
Healthcare utilization				
ndrugnames_	Number of prescription drugs the patient is on	continuous	1,2	ODB
n_md_visits_	Number of physician visits; reported as total and by categories (family practitioner and specialist)	continuous	1,2	

n_hcd_visits_	Number of home care visists; reported as total and by categories (nursing, personal support, allied health)	continuous	1,2	
nhosp_	Number of hospitalizations; reported as total and by categories (urgent and elective)	continuous	1,2	DAD
admcat_	Admission categories: urgent and elective	categorical	1,2	DAD
los	Length of stay, days	continuous	1,2	DAD
instftyp_	Institution from where admitted	categorical	1,2	DAD
instlhin_	LHIN where admitted	categorical	1,2	DAD
dx10code1-25	Diagnosis ICD10 codes for each admission	categorical	1,2	DAD
ds10type1-25	Type of diagnosis code: "M"- MRDX; "1" - preadmission; "2" - post-admission	categorical	1,2	DAD
dischdisp	Institution where discharged to	categorical	1,2	DAD
Healthcare costs				
inpat_cost_	Inpatient hospitalization Costs	continuous	1,2	DAD
sds_cost_	Same Day Surgery Costs	continuous	1,2	SDS
er_cost_	Emergency Department Costs	continuous	1,2	NACRS
odb_cost_	Costs for Ontario Drug Benefits	continuous	1,2	ODB
hc_cost_	Costs for Home Care Services	continuous	1,2	HCD
md_cost_	Physician expenditures are a combination of the costs for capitation and fees-for - services	continuous	1,2	OHIP
mh_cost_	Costs for Admissions to Mental Health Care Beds (using OMHRS)	continuous	1,2	OMHRS
onc_cost_	Oncology Clinic Costs	continuous	1,2	NACRS
dial_cost_	Dialysis Clinic Costs	continuous	1,2	NACRS
rehab_cost_	Costs for Rehabilitation	continuous	1,2	NRS
ccc_cost_	Costs for Complex Continuing Care	continuous	1,2	CCRS

lab_cost_	Costs for Laboratory investigations	continuous	1,2	OHIP
ltc_cost_	Costs for Long-Term Care	continuous	1,2	CCRS
total_cost_	Total healthcare expenditures	continuous	1,2	

Appendix 3: Approach to data analyses and adjusting for covariates

Outcome	**Type of response variable**	**Method of analysis**	**List of potential covariates,** (forward selection)
Incremental costs (total and by care category, province wide)	**Continuous**	Method of recycled predictions using generalized linear regression models with gamma distribution and the log link (incl. two-part models if needed)	**Socio -demographic factors:** Age (to be used for per LHIN analysis) Sex (to be used for per LHIN analysis) Income Urban/Rural residence Immigration status **Clinical status and care characteristics:** Number of EDCs and specific clinical clusters of interest such mental disease or dementia Access to a geriatrician Primary care group affiliation Number of physician visits (primary care and specialist) Number of home care visits
Costs per LHIN (total and by care category)		Multi-level generalized linear models with gamma distribution	
HCU rate per LHIN		Ordinary Least Squares regression model with aggregated values of covariates	
Incremental rates of healthcare use (e.g. all cause hospital admission, physician visits and home care visits, province wide)	**Count**	Method of recycled predictions using generalized linear regression model with negative binomial distribution and the log link (incl. two-part models if needed)	
Rates of healthcare use by LHIN level		Multi-level generalized linear models with negative binomial distribution	
All-cause mortality	**Categorical**	Logistic regression	

Appendix 4: ACSC conditions and codes

	Condition	ICD-10-CA Codes	Exclusions	Source
1	Angina	I20, I23.82, I24.0, I24.8, I24.9	Cardiac procedure admissions	**CIHI("Canadian Institute for Health Information: Ambulatory Care Sensitive Conditions," 2016) AHQR("AHRQ Quality Indicators—Prevention Quality Indicators Technical Specifications Updates," July 2016)**
2	Asthma	J45		
3	COPD	J41, J42, J43, J44, J47; J10.0, J11.0, J12–J16, J18, J20, J21, J22 if J44 as a secondary dx		
4	Diabetes	E10.0^^, E10.1^^, E10.63, E10.64, E10.9^^, E11.0^^, E11.1^^, E11.63, E11.64, E11.9^^, E13.0^^, E13.1^^, E13.63, E13.64, E13.9^^, E14.0^^, E14.1^^, E14.63, E14.64, E14.9^^		
5	Grand mal status and other epileptic convulsions	G40, G41		
6	Heart failure and pulmonary edema	I50, J81	Cardiac procedure admissions	
7	Hypertension	I10.0, I10.1, I11	Cardiac procedure admissions	
8	Bacterial pneumonia	J13, J14, J15211, J15212, J153, J154, J157, J159, J160, J168, J180, J181, J188, J189	Immunocompromised states and procedures#	
9	Dehydration	E860; E861, E869; (Hyperosmolality and/or hypernatremia) E870; (Gastroenteritis) A080, A0811, A0819, A082, A0831, A0832, A0839, A084, A088, A09, K5289, K529; (Acute kidney failure) N170-N172, N178, N179, N19, N990	I120, I1311, I132, N185, N186	
10	UTI	N10, N119, N12, N151, N159, N16, N2884, N2885, N2886, N3000, N3001, N3090, N3091, N390	Kidney/urinary tract disorder diagnosis codes^; Immunocompromised States and Procedures#	

1. Canadian Institute for Health Information: Ambulatory Care Sensitive Conditions 2016 [Available from: http://indicatorlibrary.cihi.ca/display/HSPIL/Ambulatory+Care+Sensitive+Conditions.
2. AHRQ Quality Indicators—Prevention Quality Indicators Technical Specifications Updates: Agency for Healthcare Research and Quality; July 2016 [Version 6.0 (ICD 10):[Available from: http://www.qualityindicators.ahrq.gov/Modules/PQI_TechSpec_ICD10_v60.aspx.

Chapter 3

Incremental Healthcare Utilization and Costs Among New Senior High Cost Users in Ontario, Canada: a retrospective matched cohort study

This chapter was submitted to BMJ Open. It keeps the corresponding format.

Sergei Muratov[1], Justin Lee[1,2], Anne Holbrook[1,3], Jason R Guertin[5,6], Lawrence Mbuagbaw[1], J Michael Paterson[6,7], Tara Gomes[6,8], Priscila Pequeno[6], Jean-Eric Tarride[1,9]

[1]Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada

[2]Division of Geriatric Medicine, Department of Medicine, McMaster University, Hamilton, Ontario, Canada

[3]Division of Clinical Pharmacology and Toxicology, Department of Medicine, McMaster University, Hamilton, Ontario, Canada

[4]Département de médecine sociale et préventive, Faculté de Médecine, Université Laval, Quebec City, Quebec, Canada

[5]Centre de recherche du CHU de Québec, Université Laval, Axe Santé des Populations et Pratiques Optimales en Santé, Québec City, QC, Canada

[6]ICES, Toronto, Ontario, Canada

[7]Department of Family Medicine, McMaster University, Hamilton, Ontario, Canada

[8]Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Ontario, Canada

[9]Center for Health Economics and Policy Analysis (CHEPA), McMaster University, Hamilton, Ontario, Canada

Corresponding author:

Sergei Muratov

Department of Health Research Methods, Evidence, and Impact, McMaster University

1280 Main Street West, Hamilton, ON L8S 4K1

muratos@mcmaster.ca

(905)523-7284

Key words: health policy, health economics, geriatrics medicine

Word count (excluding title page, abstract, references, figures and tables): 4038

Strengths

- This population-based study examines incident (new) senior high-cost users (HCU), which provides important information on the driving factors for HCU status
- Inclusion of all incident senior HCU in the province into the study population allowed us to calculate their monetary impact on the provincial healthcare budget
- This analysis includes a comprehensive spectrum of the most important cost categories that contribute to total public healthcare expenditures in the province

Limitations

- Despite the comprehensiveness of cost analyses, a few of the cost categories may not have been captured in full, e.g. outpatient intravenous chemotherapy
- The findings, especially with respect to the total incremental costs and the budget impact, are only comparable to studies with the same HCU threshold and the choice of cost categories

Authors' contributions:

SM, JET, AH, JL, JMP, TG, LM, JRG conceptualized the study. SM, JET, AH, JL, JRG, LM, JMP, TG, PP have contributed to its design. JMP, PP, TG were instrumental in creating datasets. PP provided assistance with data analysis. SM prepared the initial draft of the manuscript and revised it based on co- authors' feedback: JET, AH, JL, JMP, TG, JRG, LM, PP provided comments to the initial draft, further revisions, read and approved the final manuscript. The responsibility of study implementation lies with the principal investigator (SM) that is supported and supervised primarily by JET.

Funding Statement:

This work is supported by in-kind support from the Ontario Drug Policy Research Network (ODPRN) and by personnel awards from the Canadian Institutes of Health Research (CIHR) Drug Safety and Effectiveness Cross-Disciplinary Training (DSECT) Program, the Program for Assessment of Technology in Health (PATH), The Research Institute of St Joe's Hamilton, St Joseph's Healthcare Hamilton, and an Ontario Graduate Scholarship (OGS). The work also is supported by ICES, an independent research institute funded by the Ontario Ministry of Health and Long-Term Care (MOHLTC). ODPRN is funded by grants from the Ontario MOHLTC and the Ontario Strategy for Patient-Orientated Research (SPOR) Support Unit, which is supported by CIHR and the Province of Ontario. The opinions, results, 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. Parts of this material are based on data and information compiled and provided by the Canadian Institute for Health Information (CIHI). However, the analyses, conclusions, opinions and statements expressed herein are those of the authors and not necessarily those of CIHI.

Competing Interests: None declared.

Abstract

Objectives: To describe healthcare use and spending before and on becoming a new (incident) senior HCU compared with senior non-HCUs; to estimate the incremental costs, overall and by service category, attributable to HCU status; and to quantify its monetary impact on the provincial healthcare budget in Ontario, Canada.

Design: We conducted a retrospective, population-based comparative cohort study using administrative healthcare records. Incremental healthcare utilization and costs were determined using the method of recycled predictions allowing adjustment for pre-incident and incident year values, and covariates. Estimated budget impact was computed as the product of the mean annual total incremental cost and the number of senior HCUs.

Participants: Incident senior HCUs were defined as Ontarians aged ≥66 years who were in the top 5% of healthcare cost users during fiscal year 2013 (FY2013) but not during fiscal year 2012 (FY2012). The incident HCU cohort was matched with senior non-HCUs in a ratio of 1:3.

Results: Senior HCUs (n=175,847) reached the annual HCU threshold of $10,192 through different combinations of incurred costs. Although HCUs had higher healthcare utilization and costs at baseline compared to non-HCUs, HCU status was associated with a substantial spike in both, with prolonged hospitalizations playing a major role. Twelve percent of HCUs reached the HCU expenditure threshold without hospitalization. Compared to non-HCUs (n=527,541), HCUs incurred an additional $25,527 per patient in total healthcare costs; collectively $4.5 billion or 9% of the 2013 Ontario healthcare budget. Inpatient care had the highest incremental costs: $13,427, 53% of the total incremental spending.

Conclusions: Costs attributable to incident senior HCU status accounted for almost one-tenth of the provincial healthcare budget. Prolonged hospitalizations made a major contribution to the total incremental costs. A subgroup of patients that became HCU without hospitalization requires further investigation.

Introduction

Healthcare spending has more than doubled in the countries of the Organization for Economic Cooperation and Development (OECD) over the past two decades(World Health Organization, 2018). In Canada, where public health and health care are under provincial jurisdiction, health spending accounts for 37% of the total provincial program spending on average (Canadian Institute for Health Information, 2017). Much of the spending is disproportionately attributed to a small but heterogenous group of patients, commonly referred to as high-cost healthcare users (HCU) (Pritchard et al., 2016; Tamang et al., 2017; Wammes et al., 2018). The pressing need to control healthcare spending and the inconclusive evidence and varying success of clinical interventions targeting the HCU group (Bleich et al., 2015; J. Y. Lee et al., 2018) have prompted policy makers to revise their management strategies and to seek specific segments of the HCU population who may benefit from certain interventions more than others (Figueroa, Joynt Maddox, Beaulieu, Wild, & Jha, 2017; Karen E. Joynt et al., 2017; Tamang et al., 2017).

Incident (or new) senior HCUs represent one such segment whose patient care characteristics and spending patterns have not been well studied. A recent systematic review identified 55 studies published over the past two decades that reported HCU characteristics and healthcare utilization (Wammes et al., 2018). The vast majority (n=42) of the publications originated from the US, 9 were from Canada, 3 were generated by researchers from European countries, and 1 was from Taiwan. Compared to 9 US-based studies of the Medicare (i.e., senior) population, only the study from Taiwan among the others had a specific focus on seniors, even though approximately 45-55% of senior healthcare care resources are reportedly consumed by senior HCUs in various jurisdictions (Ku, Chiou, & Liu, 2015; Lieberman, Lee, Anderson, & Crippen, 2003; Wodchis et al., 2016). Moreover, these studies do not differentiate between prevalent (who retain the HCU status over years) and incident senior HCUs. This is important, as understanding the path to HCU status may identify opportunities for intervention(Tamang et al., 2017). Further, it is well known that senior HCUs, both prevalent and incident, generally have poor functional status and consume a high level of healthcare resources, including typically reported acute inpatient care and physician services (Holtz-Eakin, 2005; J. Y. Lee et al., 2018; Sinha, 2011). However, comprehensive descriptions of cost drivers to HCU status are few (Rais et al., 2013; Wodchis et al., 2016). A recent example is a study conducted in Ontario, the largest province in Canada, which presented a system-wide assessment of cost concentration among HCUs over 3 years using both longitudinal and cross-sectional approaches to their analysis (Wodchis et al., 2016). While providing valuable information on the transition of patients between various cost strata, their longitudinal analyses focused on the persistence of costs among all HCUs. Their cross-sectional analysis of expenditures by cost category was limited by only reporting on the top 1% of HCUs and was not stratified by age. Another poorly explored aspect of HCU cost analysis is the economic burden associated with HCU status, which remains largely unknown in Canada and elsewhere. While some international studies have compared costs between HCUs and non-HCU cohorts in a particular year using a cross-sectional design (Figueroa, Frakt, Lyon, Zhou, & Jha, 2017; Pritchard et al., 2016; Reid et al., 2003), these comparative studies did not consider any secular trends over time (e.g. costs in the years before the incident year). This limits our understanding of the true incremental costs of becoming a new HCU, especially among seniors.

We recently reported on a cohort of incident senior HCUs compared to matched non-HCUs to examine regional variation in mortality and costs in Ontario using cross-sectional data (Muratov et al., 2018). Here we aim to determine the incremental healthcare utilization and costs among new senior HCUs in Ontario by looking at the same data longitudinally. The main objectives of this study were to 1) describe healthcare use and spending before and on becoming a senior HCU compared with senior non-HCUs; 2) estimate costs and healthcare use attributable to the incident senior HCU status, and to 3) quantify the monetary impact of incident senior HCUs on the provincial healthcare budget.

Methods

Ethics Approval

This study was approved by Hamilton Integrated Research Ethics Board (ID#1715-C).

Study design

We conducted a retrospective population-based matched cohort study using administrative healthcare data from Ontario, Canada. The protocol for this research has been published(Muratov et al., 2017).

Setting and data sources

Ontario is Canada's most populous province, with almost 14 million residents (approximately 40% of the Canadian population) (Statistics Canada, 2016). The Ontario Ministry of Health and Long-Term Care (MOHLTC) pays for approximately 70% of health care provided in the province. For seniors, this proportion is higher as it includes nearly 100% of hospital care, physician services, and prescription drugs for seniors

(Canadian Institute for Health Information, 2017). Contribution to other services (e.g., long-term care) may be less (Muratov et al., 2017).

We used 2 years of linked administrative data. The Ontario government fiscal year 2013 (April 1, 2013 and March 31, 2014) was considered the incident year (FY2013). Fiscal year 2012 (FY2012: April 1, 2012 and March 31, 2013) was the baseline or pre-incident year. A patient-level dataset was created by linking 19 health administrative databases(Muratov et al., 2017) using unique encoded identifiers at ICES (www.ices.on.ca). ICES is an independent, non-profit research corporation funded by the Ontario MOHLTC.

Study population

Incident senior HCUs were defined as individuals aged 66 years or above with annual total healthcare expenditures within the top 5% threshold of all Ontarians in FY2013, who were not in the top 5% in FY2012. The 5% threshold is commonly reported in HCU studies in Canada and elsewhere (Guilcher et al., 2016; Holtz-Eakin, 2005; Riley, 2007; Wodchis et al., 2016). The >66 year age threshold was applied to capture Ontario Drug Benefit (ODB) expenditures for at least one year before the incident year: ODB coverage starts automatically when Ontarians reach 65 years of age (Ontario Ministry of Health and Long-term Care, 2018). The "non-HCU" cohort included those whose annual total health care expenditures in FY2012 and FY2013 were below the top 5% threshold in both years. The incident HCU cohort was matched with non-HCU in a ratio of 1:3 according to age at cohort entry (+/- 1 month), sex and Local Health Integration Network (LHIN) of patient residence. LHINs, Ontario's 14 regional health districts, are responsible for the planning and administration of most of hospital- and community-based health services delivered within their geographic boundaries (Ontario's LHINs, 2017).

Variables

Our dataset included key information on socio-demographic and health status, healthcare utilization and costs. Described in the study protocol (Muratov et al., 2017) in more detail, key variables are briefly summarized below.

Socio-demographic status included age, sex, low income status, and geography of residence (urban/suburban/rural). Low income status was based upon net household income reported to receive ODB subsidy in FY2012. Rurality was based on the Rurality Index for Ontario (RIO) which is a scale from 0 to 100. A RIO between 0 and 9 defined an individual from the urban area, between 10 and 40 described a suburban resident, and a resident from a rural area had a RIO score of 40 and above (Kralj B, 2000).

Health status was assessed using several variables. We used two tools derived from Johns Hopkins Adjusted Clinical Groups (ACG®) System, Version 10, a case-mix methodology to describe a population's healthcare utilization (Johns Hopkins ACG® System Version 10.0, 2014). First, the general degree of comorbidity was captured by the number of Johns Hopkins Aggregated Diagnosis Groups (ADGs): person-focused, diagnosis-based method to measure patients' illness by assigning individual ACGs into diagnosis clusters(Austin, van Walraven, Wodchis, Newman, & Anderson, 2011). A higher number of ADGs per patient indicates a greater burden of illness. In addition, we identified the proportion of patients with a history of hypertension, malignancy, and mental health condition using John Hopkins Expanded Diagnosis Clusters (EDCs). For each condition, we checked whether the patient was diagnosed with the condition in the 3 years prior to FY2013. Finally, we used validated administrative data case definitions to identify whether the patient had a history of several common chronic diseases, including congestive heart failure, diabetes, and chronic obstructive pulmonary disease (Gershon et al., 2009; Schultz, Rothwell, Chen, & Tu, 2013).

Whereas socio-demographic characteristics and health status were captured at baseline, healthcare utilization and expenditures were obtained for the full two years of study. Utilization variables included the number of hospitalizations (all, elective and unplanned), emergency department (ED) visits, physician encounters, and publicly-funded home care services. Home care services were subclassified by type of service: nursing, personal support, and allied health. For each hospitalization, we obtained the total length of stay (TLOS), in days.

Health care expenditures were estimated using ICES person-level health utilization costing algorithms (Wodchis WP, Bushmeneva K, Nikitovic M, & McKillop I, 2013), which report expenditures according to twelve health service cost categories. Hospital costs were the sum of costs associated with acute inpatient care and same-day surgery. Mental health admissions were costed separately. Physician expenditures were the sum of fee-for-service billings and capitation payments. Costs were expressed in 2013 Canadian Dollars.

Outcomes

The primary outcome measures were 1) one-year incremental healthcare utilization for hospital admissions (total and by types such as unplanned and elective), emergency visits, physician encounters (total and separately for specialists and general practitioners [GP]), and home care services (total and by type); 2) one-year incremental costs attributable to becoming an HCU (total healthcare expenditures and by cost category); and 3) provincial budget impact of new senior HCUs in FY2013. Incremental healthcare use and costs were calculated as the difference between the two cohorts over time.

Statistical analysis

Baseline patient socio-demographic and health status characteristics of the two cohorts in FY2012 were compared using the absolute standardised difference (aSD), with aSD>0.1 indicating a meaningful difference (Mamdani et al., 2005). We then described the HCU cohort in the context of cost categories and their contribution to the HCU status by calculating the proportion (%) of HCU in each cost category. Since we expected hospitalizations to be a frequent cause of new HCU status, we repeated this analysis for HCUs who were not hospitalized during the incident year to evaluate the contributions of cost drivers other than hospital admission. This was followed by a longitudinal comparison of the unadjusted healthcare use and costs in both cohorts for both the incident year and the preceding year.

Incremental healthcare use and costs were estimated using the recycled predictions method (Basu et al., 2006; Chang et al., 2017; Lange, Zeidler, & Braun, 2014; Mannino et al., 2015). Commonly used to evaluate the marginal effect of a covariate on the response variable, the method uses fitted regression models to predict incremental values of the outcomes in two hypothetical populations: one where all subjects are HCU and another where all are non-HCU, all the other covariates being the same. The difference in predicted means between the two populations indicates the incremental value. The method allows for correlation between outcome values in the year before the index year (FY2012) and after the index year (FY2013), while comparing HCU with non-HCU. Confidence intervals (CI) of the incremental values was obtained through the percentile method: random bootstrap resampling with 1000 iterations created a distribution where the 2.5th and 97.5th percentiles were the 95% lower and upper bound CIs, respectively (Mannino et al., 2015).

We used generalized linear regression to model the study outcomes. Costs were modeled with gamma distribution and log-link function to handle the right-skewed data (Basu, Manning, & Mullahy, 2004; Gregori et al., 2011). The choice of gamma distribution was confirmed by the modified Park test (Manning & Mullahy, 2001). For count data (e.g., hospital admissions or home care visits), a negative binomial (NB) distribution was specified as the leading option to better account for overdispersion (i.e., observed variance is greater than the assumed variance) (Elhai, Calhoun, & Ford, 2008; Lui WS & Cela J, 2008). In cases of a NB model not converging, Poisson distribution was used. For both costs and count data, we used two-part models (Hurdle regression) to manage zero values in the response variables: the first part used a logistic regression to predict the probability of positive values of the outcome, while a gamma or a negative binomial model was applied in the second stage for positive costs and counts, respectively (Lui WS & Cela J, 2008; Mihaylova, Briggs, O'Hagan, & Thompson, 2011). All the models were adjusted for previous resource use (e.g., costs or healthcare use in FY2012), age, sex, ADGs, and low-income status. Because our dataset included all senior HCU subjects in the province at the time of the study, we were able to estimate the total provincial public healthcare expenditures attributable to HCU status among Ontario seniors by multiplying the total incremental costs by the total number of senior HCU. Statistical analyses were conducted using SAS version 9.4.3 (SAS Institute Inc., Cary, NC).

Results

Patient characteristics

The total study population consisted of 703,388 seniors, of which 175,847 were incident HCUs. This population of incident HCUs represents 46% of all senior HCUs in FY2013 (n= 383,257) but only 9.4% of the Ontario senior population and 1.4% of the total population in the province(Statistics Canada, 2016). As expected, the mean ages of the HCU and non-HCU cohorts were identical at 77.7 years (standard deviation (SD) 7.7); 53% were women; and most resided in suburban areas (12.2 vs. 11.8, aSD=0.02) (Table 1). Compared to non-HCUs, HCUs had poorer health status as defined by both the number of aggregated diagnosis groups (10.2 vs. 7.9, aSD=0.54) and higher prevalence of chronic diseases. A relatively greater percentage of HCU cohort members had a primary care provider (97% vs. 88.6%, aSD=0.33).

Table 1 Patient characteristics

Characteristic	**HCU** (N=175,847)	**Non-HCU** (N=527,541)	**aSD**
Socio-demographics			
Age, mean (SD), yr	77.7 ± 7.7	77.7 ± 7.7	0
Sex, female	93,119 (53%)	248,040 (47.0%)	0
Rural Index of Ontario score, mean (SD)	12.2 ± 18.2	11.8 ± 18.2	0.02
Low income	31,843 (18.1%)	92,566 (17.5%)	0.01
Health Status			
# Adjusted Diagnostic Groups, mean (SD)	10.2 ± 4.0	7.9 ± 4.5	0.54
Hypertension$	110,692 (63.0%)	282,867 (53.6%)	0.19
Congestive Heart Failure#	25,195 (14.3%)	36,877 (7.0%)	0.24
Chronic Obstructive Disease Pulmonary#	48,738 (27.7%)	96,513 (18.3%)	0.23
Diabetes#	62,014 (35.3%)	138,794 (26.3%)	0.2
Myocardial infarction#	12,892 (7.3%)	24,024 (4.6%)	0.12
Rheumatoid Arthritis#	5,607 (3.2%)	9,334 (1.8%)	0.09
Malignancy$	56,855 (32.3%)	123,932 (23.5%)	0.2
Mental Health condition$	67,441 (38.4%)	144,377 (27.4%)	0.24

$- constructed based on Expanded Diagnosis Codes
#- ICES-derived cohort
SD- standard deviation; aSD- absolute standardized difference with aSD > 0.1 indicating meaningful difference between admitted and non-admitted

HCU status

The 5% HCU status threshold for this study was $10,192. As shown in Figure 1, patients could become HCU through different combinations of incurred costs. Approximately 40% of the HCU became a HCU (i.e., incurred at least $10,192 in total annual healthcare expenditures) due to a single cost category, predominantly hospital admissions (70.1%). For 13% of the HCUs, more than one cost category was above the threshold (e.g., hospital admission and rehabilitation costs). Among the remaining 47%, no single cost category was sufficient to meet the expenditure threshold for HCU status: HCU status was achieved through expenditures in several cost categories. In this case, the most common contributing categories were physician compensation, drug benefits, and hospitalization.

As many as 11.7% (N=20,501) of the HCU were not hospitalized during the incident year (Appendix 1). Their new HCU status was mainly due to a combination of physician compensation (99.8%), ODB (99.4%), and laboratory test costs (87.3%), home care (54.1%) and emergency department visits (45.3%). Of note, some of the patients within several cost categories had costs high enough for the patient to become a HCU. Examples include 72.3% of patients in long-term care, 63.4% of patients with cancer care, and 19.1% of patients with drug costs.

Dynamics of change in healthcare use and costs

Analysis of observed healthcare utilization in the two cohorts identifies an upward trajectory in health services consumption among senior HCU. As shown in Figure 2, compared to non-HCU, the HCU consumed more services in the pre-incident year across all care categories: physician encounters (mean per patient: 15.4 vs. 10.1, aSD=0.55), home care visits (mean per patient: 7.7 vs. 1.8; aSD=0.24), emergency department (ED) visits (mean per patient: 0.6 vs. 0.3; aSD=0.26), and hospital admissions (mean per patient: 0.04 vs. 0.02; aSD=0.08). This was followed by a dramatic increase in healthcare use among senior HCU during FY2013, while the service consumption among non-HCU remained relatively unchanged.

Similarly, the total public healthcare expenditures among senior HCU were higher in the pre-incident year compared to non-HCU (mean per patient: $4,166 vs. $2,372, aSD=0.74), followed by a substantial spike during the incident year ($29,784 vs. $2,471; aSD=1.33) (Figure 3). While the major drivers of total costs were analogous in the two cohorts in the year before (in descending order: drug benefits, physician costs, hospital admissions or home care), the top contributors in the HCU cohort changed during the incident year. With an annual mean of 1.07 of hospital admissions (mean TLOS: 8.8 (SD 14.8)) among senior HCU compared to a mean of 0.03 admissions (mean TLOS: 2.8 (SD 9.6)) for non-HCUs in FY2013, prolonged (i.e., lengthier compared to non-HCUs) hospitalizations were the major driver of total healthcare expenditures ($13, 558) in the incident year. These were followed by physician ($4,214) and ODB costs ($2,456). Categories such as rehabilitation, complex continuing care, dialysis, and mental health admissions were almost exclusively associated with the HCU status. Little change in the list of major cost drivers and the trajectory of costs over time was noticeable among non-HCU seniors. More detail is provided in Appendices 2 and 3.

Incremental costs and healthcare use

Table 2 shows the magnitude of incremental healthcare use by senior HCU during the incident year adjusting for the pre-incident values and other covariates. Compared to the year before becoming an HCU, unplanned hospitalizations accounted for 74% of all incremental admissions at an additional mean of 0.77 hospitalizations per HCU (95%CI: 0.77-0.78) annually. Similarly, specialist visits constituted 75% of the incremental physician encounters at an additional mean of 22.8 visits (95%CI: 22.7-22.9), whereas personal support worker visits contributed the most to the incremental home care use at additional mean of 15.6 visits (95%CI: 15.3-15.9) per HCU patient.

Table 2: Incremental healthcare use associated with HCU status, by healthcare type

Healthcare type	Annual incremental utilization, mean (95% CI)
Hospital admission, All	1.04 (1.04 -1.05)
Hospital admission, elective	0.29 (0.29 -0.3)
Hospital admission, unplanned	0.77 (0.77 -0.78)
Emergency department visits	1.4 (1.4 -1.4)
Physician visits, All	32.1 (31.9 -32.3)
General practitioner visits	9.3 (8.7 -9.5)
Specialist visits	22.8 (22.7 -22.9)
Home care services, All*	25.1 (24.4 -25.7)
Personal support	15.6 (15.3 -15.9)
Nursing	5.3 (4.9 -6.0)
Allied	1.5 (1.5 -1.6)
Other*#	2.8 (2.7 -2.9)

* - fit using Poisson distribution; all other are fit using Negative Binomial
# - "Other" includes social services, case management, and respite care
Annual incremental utilization is an additional mean number of services received by a HCU in the incident year compared with a non-HCU and the baseline year

The total annual mean adjusted costs attributable to HCU status were $25,527 (95%CI: $25,383 - $25,670) (Table 3), with hospital admissions being by far the major contributor at an additional mean of $13,428 (95%CI: $13,333 - $13,533) per HCU. Details of the regression analyses are provided in Appendices 4-5. Given the size of the senior incident HCU population (n=175,847), the estimated provincial budget impact of the senior incident HCU status was $4.5 billion (CAD). This accounts for approximately 9% of the 2013 total provincial healthcare expenditures ($51 billion) (Institute for Competitiveness & Prosperity, 2014).

Table 3: Incremental expenditures associated with HCU status, by cost component and total

Cost component	Annual incremental costs*, mean (95% CI)
Hospital admission	$ 13,428 (13,334 -13,534)
Physicians	$ 3,150 (3,134 -3,168)
Ontario Drug Benefits	$ 1,493 (1,462 -1,523)
Rehabilitation	$ 1,430 (1,392 -1,467)
Home care	$ 1,363 (1,347 -1,378)
Cancer care	$ 1,226 (1,200 -1,253)
Complex continuing care	$ 1,213 (1,168 -1,257)
Long-term care	$ 1,021 (995 -1,046)
Emergency department	$ 684 (679 -687)
Mental health admissions	$ 258 (238 -278)
Dialysis	$ 89 (79 -99)
Laboratory tests	$ 51 (50 -52)
Total incremental cost	$ 25,527 (25,383 -25,670)

*- Costs were modelled to follow gamma distribution with log-link function
Annual incremental costs are additional mean expenditures incurred by a HCU in the incident year compared with a non-HCU and the baseline year

Discussion

The study has examined a cohort of new senior HCU patients compared with matched non-HCUs focusing on the absolute and incremental comparative healthcare use and expenditures before and after HCU conversion. We determined that although senior HCUs were already on an upward trajectory during the year before HCU status, showing higher healthcare utilization and costs in the pre-incident year, the HCU status was associated with a spike in healthcare expenditures. We found that seniors became HCU through incurring costs in various combinations, although half of the senior HCU could reach the HCU status by incurring costs from only one or two categories reaching the threshold, mainly prolonged hospitalization. Approximately 12% of HCUs who had no hospitalization in the incident year achieved HCU status through incurring a combination of predominantly physician, ODB, and laboratory test costs. Compared to non-HCU, senior HCU incurred an additional $25,527 per patient in total incremental public healthcare expenditures and cost almost one-tenth of the provincial budget in the incident year. Hospitalizations, physician compensation and ODB were responsible for the highest incremental costs.

This study fills a current gap in the HCU economic literature, especially Canadian HCU studies where few of them have focused on seniors or used a comparative group of non-HCUs. Also, as opposed to cross-sectional studies that are common in the area of HCU research, we were able to capture the economic burden attributable to HCU status among senior Ontarians using longitudinal data. Our approach of the recycled predictions has allowed us to compare the healthcare use and costs between HCUs and a matched cohort of non-HCUs while taking account of the correlation between the pre- and post values, managing excessive zero values by developing two-part models, and adjusting for confounding by including important socio-demographic and health status covariates in the models. Another option we considered was the difference in differences (DID) estimator (Dimick & Ryan, 2014; Stock JH & Watson MW, ; 2011). Frequently employed by economists to assess the impact of introducing a policy or a change in the system, its use is however conditional on two major assumptions that need to be met: parallel trends and no group variation at baseline. While the latter could be dealt with using statistical adjustment, the former assumes that trajectories in outcomes (i.e., costs and use) between the groups are the same prior to the exposure (i.e., HCU conversion). Because we only had access to one year of data prior to the incident year (i.e., the baseline year) by design, it was not possible to determine the trajectories between the cohorts.

Consistent with 9 studies of senior HCUs identified by Wammes et al., our results confirm the high prevalence of common conditions among senior HCUs, the important impact of inpatient care costs, the increasing role of home and long-term care in the HCU cost profile. Some studies also mention non-hospitalized senior HCUs without providing their detailed description (N. S. Lee, Whitman, Vakharia, Ph, & Rothberg, 2017; Wodchis et al., 2016). Our findings are however challenging to compare with these for several reasons. First, in addition to the incremental values, we provide a comprehensive assessment of costs and healthcare utilization for a specific segment of the HCU population: senior incident cases. To our knowledge, no other studies have examined this specific patient population, especially in such detail (Wammes et al., 2018). Second, as Wammes et el. show, the HCU threshold used in the US and other countries (e.g., Denmark and Germany) is often 10%, while Canadian studies commonly apply the 5% threshold (Wammes et al., 2018). Third, the spectrum of cost categories included in analysis may vary between countries and even provinces in Canada. Prescription drug costs, for example, the source of one of the highest incremental values in our study, were not covered by the US Medicare program (which covers senior patients) until 2003, although the launch of a fully developed program was delayed until mid-2000s (Oliver, Lee, & Lipton, 2004; Y. Zhang, Donohue, Newhouse, & Lave, 2009), limiting the comparability of earlier studies that relied only on Medicare payments (Ganguli, Thompson, & Ferris, 2017; Lieberman et al., 2003; Riley, 2007). In this respect, our efforts to standardize cost analyses by using a costing methodology that allows obtaining patient-level expenditures from multiple sources in one standard way is a step toward higher comparability of future studies.

Strengths and limitations

Our study has several strengths. First, the study is population-based, including all incident senior HCU in the province. Second, the study examines incident HCU, which provides important information on the driving factors for HCU status. Third, we included a comprehensive spectrum of the most important cost categories that contribute to total public healthcare expenditures in the province.

The study also has important limitations. The nature of methodology applied to calculate the costs was different across various cost categories. As opposed to the nominal costs per visit (e.g., physician or home care) or prescription claim, some of the costs were estimations, e.g. a provincial average cost per case of inpatient care weighted for resource intensity (Walter P. Wodchis, Bushmeneva K, Nikitovic M, & McKillop I, 2013). However, when used for comparisons at a provincial level, these estimations are considered acceptable (Walter P. Wodchis et al., 2013). Also, despite our comprehensive coverage of cost categories, some public healthcare expenditures are not accounted for. Examples include community services (e.g., community services for elderly) and public health costs. In addition, a few of the cost categories included the analysis may not be captured in full. Most notably, we did not have access to the costs of outpatient intravenous chemotherapy, which can be costly (Claire de Oliveira et al., 2013). Despite these limitations, it is unlikely that the unaccounted costs for individual healthcare services amount to more than 5-8% of total public expenditures on healthcare in seniors (Muratov S et al., 2018; Wodchis et al., 2016). At the same time, the true hospitalization expenses may be underestimated as physician billings for inpatient services are currently captured by a separate cost category which makes our estimates of the hospital costs conservative. Finally, different HCU threshold may yield different estimations of the incremental costs. Although ours is the most commonly used HCU threshold in Canada (Wammes et al., 2018), our findings are largely comparable to studies with the same threshold and the choice of cost categories.

Despite these limitations, our findings have policy and research implications. There is currently no clear internationally accepted definition of the HCU (J. Y. Lee et al., 2018). They are also referred to by many names (e.g., heavy, frequent or high needs users) that are used interchangeably with HCU (J. Y. Lee et al., 2018). However, our data shows that frequent users of healthcare may not be synonymous with high-cost users of healthcare and both need to be distinguished. One prolonged hospital stay, for example, can drive a senior patient to become a HCU. Although interventions have been introduced to either prevent or divert such hospitalizations, their success is unclear (J. Y. Lee et al., 2018). Further efforts are needed to examine predictors at the pre-hospital level and to identify actionable cost drivers during admission. At the same time, more than one tenth of senior HCUs had no hospital costs. The latter subset of HCUs requires further investigation. Reducing ODB expenditures by exploring pharmaceutical policy or pricing strategies (e.g. generic drug tendering) stands out as a promising but challenging area to achieve potential cost reductions (Morgan S & Persaud N). Canada has recently made steps to alleviate the burden of drug costs by negotiating lower prices of generic and non-generic drugs with manufacturers (The pan-Canadian Pharmaceutical Alliance. Council of the Federation, 2018). Although there may be room for further savings among generic drugs (Morgan & Persaud, 2018), these may be offset by the growing share of expensive biologics coupled with just a modest uptake of biosimilars (Lungu E. & Warwick G). Finally, future cost analysis of senior HCUs could benefit from greater data granularity. Following a patient by type of care received in the incident year, for example, it may be possible to more precisely identify the point of HCU conversion, differentiate between outpatient and inpatient costs that contribute to it, and allocate costs more precisely.

Conclusion

Costs attributable to incident senior HCU status accounted for almost one-tenth of the provincial budget. Prolonged hospitalizations made a major contribution to the total incremental costs. However, categories such as physician billings, drug benefits and other, in various combinations, also were important. A subgroup of patients that became HCU without hospitalization requires further investigation.

References

AHRQ Quality Indicators—Prevention Quality Indicators Technical Specifications Updates. (July 2016). Version 6.0 (ICD 10). Retrieved from http://www.qualityindicators.ahrq.gov/Modules/PQI_TechSpec_ICD10_v60.aspx

An, S. J., Kim, T. J., & Yoon, B. W. (2017). Epidemiology, Risk Factors, and Clinical Features of Intracerebral Hemorrhage: An Update. *J Stroke, 19*(1), 3-10. doi:10.5853/jos.2016.00864

Austin, P. C., van Walraven, C., Wodchis, W. P., Newman, A., & Anderson, G. M. (2011). Using the Johns Hopkins Aggregated Diagnosis Groups (ADGs) to predict mortality in a general adult population cohort in Ontario, Canada. *Med Care, 49*(10), 932-939. doi:10.1097/MLR.0b013e318215d5e2

Basu, A., Arondekar, B. V., & Rathouz, P. J. (2006). Scale of interest versus scale of estimation: comparing alternative estimators for the incremental costs of a comorbidity. *Health Econ, 15*(10), 1091-1107. doi:10.1002/hec.1099

Basu, A., Manning, W. G., & Mullahy, J. (2004). Comparing alternative models: log vs Cox proportional hazard? *Health Econ, 13*(8), 749-765. doi:10.1002/hec.852

Bleich, S. N., Sherrod, C., Chiang, A., Boyd, C., Wolff, J., DuGoff, E., . . . Anderson, G. (2015). Systematic Review of Programs Treating High-Need and High-Cost People With Multiple Chronic Diseases or Disabilities in the United States, 2008–2014. *Preventing Chronic Disease, 12*, E197. doi:10.5888/pcd12.150275

Blumenthal, D., Chernof, B., Fulmer, T., Lumpkin, J., & Selberg, J. (2016). Caring for High-Need, High-Cost Patients - An Urgent Priority. *N Engl J Med, 375*(10), 909-911. doi:10.1056/NEJMp1608511

Canadian Institute for Health Information. (2017). *National Health Expenditure Trends, 1975 to 2017*. Retrieved from Ottawa, ON: https://www.cihi.ca/en/national-health-expenditure-trends

Canadian Institute for Health Information: Ambulatory Care Sensitive Conditions. (2016). Retrieved from http://indicatorlibrary.cihi.ca/display/HSPIL/Ambulatory+Care+Sensitive+Conditions

Central Midlands NHS. (2014). *The Total Cost of Care for Older People in Solihull - an Analysis of Combined NHS and Social Care Data*. Retrieved from https://solihullccg.nhs.uk/publications/1245-bcf-cost-of-care/file

Chaix, B., Merlo, J., & Chauvin, P. (2005). Comparison of a spatial approach with the multilevel approach for investigating place effects on health: the example of healthcare utilisation in France. *J Epidemiol Community Health, 59*(6), 517-526. doi:10.1136/jech.2004.025478

Chang, C., Lee, S. M., Choi, B. W., Song, J. H., Song, H., Jung, S., . . . Suh, D. C. (2017). Costs Attributable to Overweight and Obesity in Working Asthma Patients in the United States. *Yonsei Med J, 58*(1), 187-194. doi:10.3349/ymj.2017.58.1.187

Clark, D., Armstrong, M., Allan, A., Graham, F., Carnon, A., & Isles, C. (2014). Imminence of death among hospital inpatients: Prevalent cohort study. *Palliat Med, 28*(6), 474-479. doi:10.1177/0269216314526443

Clough, J. D., Riley, G. F., Cohen, M., Hanley, S. M., Sanghavi, D., DeWalt, D. A., . . . Conway, P. H. (2016). Patterns of care for clinically distinct segments of high cost Medicare beneficiaries. *Healthc (Amst), 4*(3), 160-165. doi:10.1016/j.hjdsi.2015.09.005

D'Errigo, P., Tosti, M. E., Fusco, D., Perucci, C. A., & Seccareccia, F. (2007). Use of hierarchical models to evaluate performance of cardiac surgery centres in the Italian CABG outcome study. *BMC Med Res Methodol, 7*, 29. doi:10.1186/1471-2288-7-29

Dattalo, M., Nothelle, S., & Chapman, E. N. (2016). Targeting Enhanced Services Toward High-Cost, High-Need Medicare Patients *New Directions in Geriatric Medicine Concepts, Trends, and Evidence-Based Practice* (pp. 13-30).

de Oliveira, C., Bremner, K. E., Pataky, R., Gunraj, N., Chan, K., Peacock, S., & Krahn, M. D. (2013). Understanding the costs of cancer care before and after diagnosis for the 21 most common cancers in Ontario: a population-based descriptive study. *CMAJ Open, 1*(1), E1-E8. doi:10.9778/cmajo.20120013

de Oliveira, C., Cheng, J., Vigod, S., Rehm, J., & Kurdyak, P. (2016). Patients With High Mental Health Costs Incur Over 30 Percent More Costs Than Other High-Cost Patients. *Health Aff (Millwood), 35*(1), 36-43. doi:10.1377/hlthaff.2015.0278

Del Gobbo, L. C., Kalantarian, S., Imamura, F., Lemaitre, R., Siscovick, D. S., Psaty, B. M., & Mozaffarian, D. (2015). Contribution of Major Lifestyle Risk Factors for Incident Heart Failure in Older Adults: The Cardiovascular Health Study. *Jacc. Heart Failure, 3*(7), 520-528. doi:10.1016/j.jchf.2015.02.009

Densen, P. M., Shapiro, S., & Einhorn, M. (1959). Concerning High and Low Utilizers of Service in a Medical Care Plan, and the Persistence of Utilization Levels over a Three Year Period. *The Milbank Memorial Fund Quarterly, 37*(3), 217-250. doi:10.2307/3348768

Dimick, J. B., & Ryan, A. M. (2014). Methods for evaluating changes in health care policy: the difference-in-differences approach. *JAMA, 312*(22), 2401-2402. doi:10.1001/jama.2014.16153

Dong, G., Harris, R., Jones, K., & Yu, J. (2015). Multilevel Modelling with Spatial Interaction Effects with Application to an Emerging Land Market in Beijing, China. *PLoS One, 10*(6), e0130761. doi:10.1371/journal.pone.0130761

Elhai, J. D., Calhoun, P. S., & Ford, J. D. (2008). Statistical procedures for analyzing mental health services data. *Psychiatry Res, 160*(2), 129-136. doi:10.1016/j.psychres.2007.07.003

Figueroa, J. F., Frakt, A. B., Lyon, Z. M., Zhou, X., & Jha, A. K. (2017). Characteristics and spending patterns of high cost, non-elderly adults in Massachusetts. *Healthc (Amst), 5*(4), 165-170. doi:10.1016/j.hjdsi.2017.05.001

Figueroa, J. F., Joynt Maddox, K. E., Beaulieu, N., Wild, R. C., & Jha, A. K. (2017). Concentration of Potentially Preventable Spending Among High-Cost Medicare Subpopulations: An Observational Study. *Ann Intern Med, 167*(10), 706-713. doi:10.7326/m17-0767

Fitzpatrick, T., Rosella, L. C., Calzavara, A., Petch, J., Pinto, A. D., Manson, H., . . . Wodchis, W. P. (2015). Looking Beyond Income and Education: Socioeconomic Status Gradients Among Future High-Cost Users of Health Care. *Am J Prev Med, 49*(2), 161-171. doi:10.1016/j.amepre.2015.02.018

Fowler, R., & Hammer, M. (2013). End-of-life care in Canada. *Clin Invest Med, 36*(3), E127-132.

Ganguli, I., Thompson, R. W., & Ferris, T. G. (2017). What can five high cost patients teach us about healthcare spending? *Healthc (Amst), 5*(4), 204-213. doi:10.1016/j.hjdsi.2016.12.004

Gershon, A. S., Wang, C., Guan, J., Vasilevska-Ristovska, J., Cicutto, L., & To, T. (2009). Identifying individuals with physcian diagnosed COPD in health administrative databases. *Copd, 6*(5), 388-394.

Glazier RH, Z. B., Rayner J. (2012.). *Comparison of Primary Care Models in Ontario by Demographics, Case Mix and Emergency Department Use, 2008/09 to 2009/10.* Retrieved from Toronto:

Graverholt, B., Riise, T., Jamtvedt, G., Ranhoff, A. H., Kruger, K., & Nortvedt, M. W. (2011). Acute hospital admissions among nursing home residents: a population-based observational study. *BMC Health Serv Res, 11*, 126. doi:10.1186/1472-6963-11-126

Gregori, D., Petrinco, M., Bo, S., Desideri, A., Merletti, F., & Pagano, E. (2011). Regression models for analyzing costs and their determinants in health care: an introductory review. *Int J Qual Health Care, 23*(3), 331-341. doi:10.1093/intqhc/mzr010

Guilcher, S. J., Bronskill, S. E., Guan, J., & Wodchis, W. P. (2016). Who Are the High-Cost Users? A Method for Person-Centred Attribution of Health Care Spending. *PLoS One, 11*(3), e0149179. doi:10.1371/journal.pone.0149179

Hay, C., Pacey, M., Bains, N., & Ardal, S. (2010). Understanding the Unattached Population in Ontario: Evidence from the Primary Care Access Survey (PCAS). *Healthc Policy, 6*(2), 33-47.

Hensel, J. M., Taylor, V. H., Fung, K., & Vigod, S. N. (2016). Rates of Mental Illness and Addiction among High-Cost Users of Medical Services in Ontario. *Can J Psychiatry, 61*(6), 358-366. doi:10.1177/0706743716644764

Holtz-Eakin, D. (2005). High-Cost Medicare Beneficiaries Retrieved from http://www.cbo.gov/publication/16487

Hosmer DW, & Lemeshow S. (2000). *Applied Logistic Regression (2nd Edition)*. New York, NY: John Wiley & Sons.

Institute for Competitiveness & Prosperity. (2014). Building Better Health Care: Policy opportunities for Ontario. *Working Paper 20.* Retrieved from https://www.competeprosper.ca/uploads/WP20_BetterHealthCare_FINAL.pdf

Jayaraman, J., & Joseph, K. (2013). Determinants of place of death: a population-based retrospective cohort study. *BMC Palliat Care, 12*, 19. doi:10.1186/1472-684x-12-19

Johns Hopkins ACG® System Version 10.0. (2014). Technical Reference Guide.

Joynt, K. E., Figueroa, J. F., Beaulieu, N., Wild, R. C., Orav, E. J., & Jha, A. K. (2017). Segmenting high-cost Medicare patients into potentially actionable cohorts. *Healthcare, 5*(1), 62-67. doi:https://doi.org/10.1016/j.hjdsi.2016.11.002

Joynt, K. E., Gawande, A. A., Orav, E. J., & Jha, A. K. (2013). Contribution of preventable acute care spending to total spending for high-cost Medicare patients. *JAMA, 309*(24), 2572-2578. doi:10.1001/jama.2013.7103

Klingler, C., in der Schmitten, J., & Marckmann, G. (2016). Does facilitated Advance Care Planning reduce the costs of care near the end of life? Systematic review and ethical considerations. *Palliat Med, 30*(5), 423-433. doi:10.1177/0269216315601346

Kralj B. (2000). Measuring 'rurality' for purposes of health-care planning: an empirical measure for Ontario. *Ontario Medical Review, October*, 33-52.

Kramer, A. A., & Zimmerman, J. E. (2007). Assessing the calibration of mortality benchmarks in critical care: The Hosmer-Lemeshow test revisited. *Crit Care Med, 35*(9), 2052-2056. doi:10.1097/01.ccm.0000275267.64078.b0

Ku, L. J., Chiou, M. J., & Liu, L. F. (2015). Variations in the persistence of health expenditures and the implications for the design of capitation payments in Taiwan. *J Health Serv Res Policy, 20*(3), 146-153. doi:10.1177/1355819615577711

Lange, A., Zeidler, J., & Braun, S. (2014). One-year disease-related health care costs of incident vertebral fractures in osteoporotic patients. *Osteoporos Int, 25*(10), 2435-2443. doi:10.1007/s00198-014-2776-4

Lavergne RM. (2015). *Regional variation in Alternate Level of Care (ALC) service use in British Columbia hospitals: An opportunity for intervention?* Retrieved from Institute for Health System Transformation & Sustainability; :

Lee, J. Y., Muratov, S., Tarride, J. E., & Holbrook, A. M. (2018). Managing High-Cost Healthcare Users: The International Search for Effective Evidence-Supported Strategies. *J Am Geriatr Soc*. doi:10.1111/jgs.15257

Lee, N. S., Whitman, N., Vakharia, N., Ph, D. G., & Rothberg, M. B. (2017). High-Cost Patients: Hot-Spotters Don't Explain the Half of It. *J Gen Intern Med, 32*(1), 28-34. doi:10.1007/s11606-016-3790-3

Lieberman, S. M., Lee, J., Anderson, T., & Crippen, D. L. (2003). Reducing the growth of Medicare spending: geographic versus patient-based strategies. *Health Aff (Millwood), Suppl Web Exclusives*, W3-603-613.

Lim, J.-S., & Kwon, H.-M. (2010). Risk of "silent stroke" in patients older than 60 years: risk assessment and clinical perspectives. *Clinical Interventions in Aging, 5*, 239-251.

Lui WS, & Cela J. (2008). Count Data Models in SAS. Retrieved from http://www2.sas.com/proceedings/forum2008/371-2008.pdf

Lungu E., & Warwick G. Potential Savings from Biosimilars in Canada. *Presentation in 2017 CADTH Symposium.* Retrieved from https://www.cadth.ca/sites/default/files/symp-2017/presentations/april24-2017/Concurrent-Session-B4-Gary-Warwick.pdf

MacKenzie, T. A., Grunkemeier, G. L., Grunwald, G. K., O'Malley, A. J., Bohn, C., Wu, Y., & Malenka, D. J. (2015). A primer on using shrinkage to compare in-hospital mortality between centers. *Ann Thorac Surg, 99*(3), 757-761. doi:10.1016/j.athoracsur.2014.11.039

Mamdani, M., Sykora, K., Li, P., Normand, S.-L. T., Streiner, D. L., Austin, P. C., . . . Anderson, G. M. (2005). Reader's guide to critical appraisal of cohort studies: 2. Assessing potential for confounding. *BMJ : British Medical Journal, 330*(7497), 960-962.

Mandrekar JN, & SJ, M. (2004). *An introduction to matching and its application using SAS (Proceedings of the Twenty-ninth Annual SAS Users Group International Conference, 29, 208 'Statistics and Data Analysis').*

Manning, W. G., & Mullahy, J. (2001). Estimating log models: to transform or not to transform? *J Health Econ, 20*(4), 461-494.

Mannino, D. M., Higuchi, K., Yu, T. C., Zhou, H., Li, Y., Tian, H., & Suh, K. (2015). Economic Burden of COPD in the Presence of Comorbidities. *Chest, 148*(1), 138-150. doi:10.1378/chest.14-2434

Marchildon, G. P., & Hutchison, B. (2016). Primary care in Ontario, Canada: New proposals after 15 years of reform. *Health Policy, 120*(7), 732-738. doi:https://doi.org/10.1016/j.healthpol.2016.04.010

McCarthy D, Ryan J, & Klein S. (2015). Models of Care for High-Need, High-Cost Patients: An Evidence Synthesis. . *The Commonwealth Fund. Issue Brief.*

Mihaylova, B., Briggs, A., O'Hagan, A., & Thompson, S. G. (2011). Review of statistical methods for analysing healthcare resources and costs. *Health Econ, 20*(8), 897-916. doi:10.1002/hec.1653

Mondor, L., Walker, K., Bai, Y. Q., & Wodchis, W. P. (2017). Use of hospital-related health care among Health Links enrollees in the Central Ontario health region: a propensity-matched difference-in-differences study. *CMAJ Open, 5*(4), E753-E759. doi:10.9778/cmajo.20170054

Morgan S, & Persaud N. Generic drug prices could drop – if rebates are replaced with public tendering. Retrieved from https://healthydebate.ca/opinions/generic-drug-prices

Morgan, S. G., & Persaud, N. (2018). New generic pricing scheme maintains high prices and risks of shortages. *CMAJ, 190*(14), E410-e411. doi:10.1503/cmaj.180197

Motiwala, S. S., Croxford, R., Guerriere, D. N., & Coyte, P. C. (2006). Predictors of place of death for seniors in Ontario: a population-based cohort analysis. *Can J Aging, 25*(4), 363-371.

Muratov S, Lee J, Holbrook A, Paterson JM, Guertin JR, Mbuagbaw L, . . . TarrideJE. (2018). Regional Variation in Healthcare Spending and Mortality among Senior High-Cost Healthcare Users in Ontario, Canada: a retrospective matched cohort study. *BMC Geriatr*.

Muratov, S., Lee, J., Holbrook, A., Costa, A., Paterson, J. M., Guertin, J. R., . . . Tarride, J. E. (2018). Regional variation in healthcare spending and mortality among senior high-cost healthcare users in Ontario, Canada: a retrospective matched cohort study. *BMC Geriatr, 18*(1), 262. doi:10.1186/s12877-018-0952-7

Muratov, S., Lee, J., Holbrook, A., Paterson, J. M., Guertin, J. R., Mbuagbaw, L., . . . Tarride, J. E. (2017). Senior high-cost healthcare users' resource utilization and outcomes: a protocol of a retrospective matched cohort study in Canada. *BMJ Open, 7*(12), e018488. doi:10.1136/bmjopen-2017-018488

Nelson, L. (2012). *Lessons from Medicare's Demonstration Projectson Disease Management and Care Coordination*. Retrieved from Washington, D.C.:

Oliver, T. R., Lee, P. R., & Lipton, H. L. (2004). A Political History of Medicare and Prescription Drug Coverage. *Milbank Q, 82*(2), 283-354. doi:10.1111/j.0887-378X.2004.00311.x

Ontario's LHINs. (2017). Ontario's Local Health Integration Networks. Retrieved from www.lhins.on.ca

Ontario Ministry of Health and Long-term Care. (2018). Understadning Ontario's Drug Programs. Retrieved from http://www.health.gov.on.ca/en/public/programs/drugs/

Ouédraogo, A. M., Crighton, E. J., Sawada, M., To, T., Brand, K., & Lavigne, E. (2018). Exploration of the spatial patterns and determinants of asthma prevalence and health services use in Ontario using a Bayesian approach. *PLoS One, 13*(12), e0208205. doi:10.1371/journal.pone.0208205

Palmer, K. S., Brown, A. D., Evans, J. M., Marani, H., Russell, K. K., Martin, D., & Ivers, N. M. (2018). Standardising costs or standardising care? Qualitative evaluation of the implementation and impact of a hospital funding reform in Ontario, Canada. *Health Research Policy and Systems, 16*(1), 74. doi:10.1186/s12961-018-0353-6

Peikes, D., Chen, A., Schore, J., & Brown, R. (2009). Effects of care coordination on hospitalization, quality of care, and health care expenditures among Medicare beneficiaries: 15 randomized trials. *JAMA, 301*(6), 603-618. doi:10.1001/jama.2009.126

Pocock, S. J., Wang, D., Pfeffer, M. A., Yusuf, S., McMurray, J. J., Swedberg, K. B., . . . Granger, C. B. (2006). Predictors of mortality and morbidity in patients with chronic heart failure. *Eur Heart J, 27*(1), 65-75. doi:10.1093/eurheartj/ehi555

Pritchard, D., Petrilla, A., Hallinan, S., Jr., D. H. T., Schabert, V. F., & Dubois, R. W. (2016). What Contributes Most to High Health Care Costs? Health Care Spending in High Resource Patients. *Journal of Managed Care & Specialty Pharmacy, 22*(2), 102-109. doi:10.18553/jmcp.2016.22.2.102

Rais, S., Nazerian, A., Ardal, S., Chechulin, Y., Bains, N., & Malikov, K. (2013). High-cost users of Ontario's healthcare services. *Healthc Policy, 9*(1), 44-51.

Reid, R., Evans, R., Barer, M., Sheps, S., Kerluke, K., McGrail, K., . . . Pagliccia, N. (2003). Conspicuous consumption: characterizing high users of physician services in one Canadian province. *J Health Serv Res Policy, 8*(4), 215-224. doi:10.1258/135581903322403281

Riley, G. F. (2007). Long-term trends in the concentration of Medicare spending. *Health Aff (Millwood), 26*(3), 808-816. doi:10.1377/hlthaff.26.3.808

ROC analysis using validation data and cross validation. SAS Support. © SAS Institute Inc. Retrieved from http://support.sas.com/kb/39/724.html

Roemer, M. I., & Myers, G. W. (1956). Multiple Admissions to Hospital. *Canadian Journal of Public Health / Revue Canadienne de Sante'e Publique, 47*(11), 469-481.

Ronald, L. A., McGregor, M. J., McGrail, K. M., Tate, R. B., & Broemling, A. M. (2008). Hospitalization rates of nursing home residents and community-dwelling seniors in British Columbia. *Can J Aging, 27*(1), 109-115. doi:10.3138/cja.27.1.109

Ronksley, P. E., Kobewka, D. M., McKay, J. A., Rothwell, D. M., Mulpuru, S., & Forster, A. J. (2016). Clinical characteristics and preventable acute care spending among a high cost inpatient population. *BMC Health Serv Res, 16*, 165. doi:10.1186/s12913-016-1418-2

Roos, N. P., Shapiro, E., & Tate, R. (1989). Does a small minority of elderly account for a majority of health care expenditures? A sixteen-year perspective. *Milbank Q, 67*(3-4), 347-369.

Rosella, L. C., Fitzpatrick, T., Wodchis, W. P., Calzavara, A., Manson, H., & Goel, V. (2014). High-cost health care users in Ontario, Canada: demographic, socio-economic, and health status characteristics. *BMC Health Serv Res, 14*, 532. doi:10.1186/s12913-014-0532-2

Schootman, M., Chien, L., Yun, S., & Pruitt, S. L. (2016). Explaining large mortality differences between adjacent counties: a cross-sectional study. *BMC Public Health, 16*, 681. doi:10.1186/s12889-016-3371-8

Schultz, S. E., Rothwell, D. M., Chen, Z., & Tu, K. (2013). Identifying cases of congestive heart failure from administrative data: a validation study using primary care patient records. *Chronic Dis Inj Can, 33*(3), 160-166.

Shao X, & L, L. (2011). *Data-driven Multi-touch Attribution Models*. Paper presented at the Proceedings of the 17th ACM SIGKDD International Conference on Knowledge Discovery and Data Mining, San Diego, CA, USA. http://delivery.acm.org/10.1145/2030000/2020453/p258-shao.pdf?ip=130.113.109.55&id=2020453&acc=ACTIVE%20SERVICE&key=FD0067F557510FFB%2ED816932E3DB0B89D%2E4D4702B0C3E38B35%2E4D4702B0C3E38B35&__acm__=1543530707_9b88c33e3d7b4ae8fc446032c3bde664

Sinha, S. K. (2011). Why the elderly could bankrupt Canada and how demographic imperatives will force the redesign of acute care service delivery. *Healthc Pap, 11*(1), 46-51; discussion 86-91.

Stanton MW, R. M. (2006). *High Concentration of US Health Expenditures*. Retrieved from https://meps.ahrq.gov/data_files/publications/ra19/ra19.pdf

Statistics Canada. (2016). Population by year, by province and territory. Retrieved from http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/demo02a-eng.htm

Stock JH, & Watson MW. (; 2011). *Introduction to Econometrics* (3rd ed.): Pearson.

Sutherland JM, & Crump, R. T. (2011). *Exploring alternative level of care (ALC) and the role of funding policies: an evolving evidence base for Canada* Retrieved from https://www.cfhi-fcass.ca

Sutherland, J. M., & Crump, R. T. (2013). Alternative level of care: Canada's hospital beds, the evidence and options. *Healthc Policy, 9*(1), 26-34.

Sweetman A, & Buckley G. (2014). *Ontario's Experiment with Primary Care Reform*. Retrieved from University of Calgary:

Tamang, S., Milstein, A., Sørensen, H. T., Pedersen, L., Mackey, L., Betterton, J.-R., . . . Shah, N. (2017). Predicting patient 'cost blooms' in Denmark: a longitudinal population-based study. *BMJ Open, 7*(1), e011580. doi:10.1136/bmjopen-2016-011580

Teno, J. M., Gozalo, P. L., Bynum, J. W., & et al. (2013). Change in end-of-life care for medicare beneficiaries: Site of death, place of care, and health care transitions in 2000, 2005, and 2009. *JAMA, 309*(5), 470-477. doi:10.1001/jama.2012.207624

The pan-Canadian Pharmaceutical Alliance. Council of the Federation. (2018). . Retrieved from http://www.canadaspremiers.ca/pan-canadian-pharmaceutical-alliance/

Vang, Z. M., Sigouin, J., Flenon, A., & Gagnon, A. (2017). Are immigrants healthier than native-born Canadians? A systematic review of the healthy immigrant effect in Canada. *Ethn Health, 22*(3), 209-241. doi:10.1080/13557858.2016.1246518

Wallace, E., Stuart, E., Vaughan, N., Bennett, K., Fahey, T., & Smith, S. M. (2014). Risk prediction models to predict emergency hospital admission in community-dwelling adults: a systematic review. *Med Care, 52*(8), 751-765. doi:10.1097/mlr.0000000000000171

Walter P. Wodchis, Bushmeneva K, Nikitovic M, & McKillop I. (2013). *Guidelines on Person-Level Costing Using Administrative Databases in Ontario*. Retrieved from

Wammes, J. J. G., van der Wees, P. J., Tanke, M. A. C., Westert, G. P., & Jeurissen, P. P. T. (2018). Systematic review of high-cost patients' characteristics and healthcare utilisation. *BMJ Open, 8*(9), e023113. doi:10.1136/bmjopen-2018-023113

Wodchis WP. *The Concentration of Health Care Spending: Little Ado (yet) About Much (money). Presented at the Canadian Association for Health Services and Policy Research (CASHPR) 2012 Conference. Available at: https://www.cahspr.ca/web/uploads/presentations/C6.1_Walter_P._Wodchis.pdf. Accessed October 1, 2015*. Available at: https://www.cahspr.ca/web/uploads/presentations/C6.1_Walter_P._Wodchis.pdf.

Wodchis WP, Bushmeneva K, Nikitovic M, & McKillop I. (2013). *Guidelines on Person-Level Costing Using Administrative Databases in Ontario*. Retrieved from

Wodchis, W. P., Austin, P. C., & Henry, D. A. (2016). A 3-year study of high-cost users of health care. *CMAJ, 188*(3), 182-188. doi:10.1503/cmaj.150064

Woolf, A. D., & Åkesson, K. (2003). Preventing fractures in elderly people. *BMJ : British Medical Journal, 327*(7406), 89-95.

World Health Organization. (2018). Global Health Expenditure Database, 2000-2015. . Retrieved from http://apps.who.int/nha/database/ViewData/Indicators/en

Yan, S., Kwan, Y. H., Tan, C. S., Thumboo, J., & Low, L. L. (2018). A systematic review of the clinical application of data-driven population segmentation analysis. *BMC Med Res Methodol, 18*(1), 121. doi:10.1186/s12874-018-0584-9

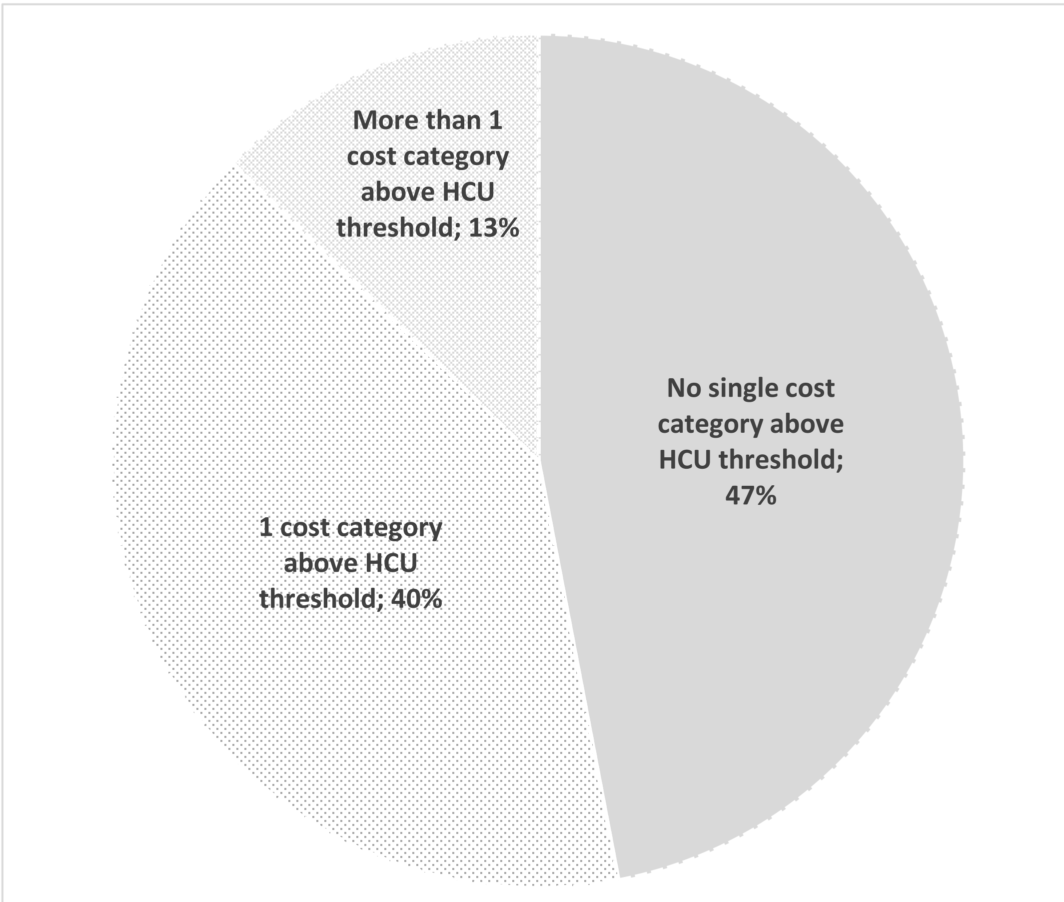
Yusuf, S., Hawken, S., Ounpuu, S., Dans, T., Avezum, A., Lanas, F., . . . Lisheng, L. (2004). Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet, 364*(9438), 937-952. doi:10.1016/s0140-6736(04)17018-9

Zhang, M., Strawderman, R. L., Cowen, M. E., & Wells, M. T. (2006). Bayesian Inference for a Two-Part Hierarchical Model. *Journal of the American Statistical Association, 101*(475), 934-945. doi:10.1198/016214505000001429

Zhang, X. (2018). Application of discrete event simulation in health care: a systematic review. *BMC Health Services Research, 18*(1), 687. doi:10.1186/s12913-018-3456-4

Zhang, Y., Donohue, J. M., Newhouse, J. P., & Lave, J. R. (2009). The Effects Of The Coverage Gap On Drug Spending: A Closer Look At Medicare Part D. *Health Aff (Millwood), 28*(2), w317-w325. doi:10.1377/hlthaff.28.2.w317

Figure 1: Proportion of new HCUs that made the HCU threshold due to various types of costs



The graph presents the proportion of senior HCU in the context of cost categories that reached the HCU threshold of $10,192.

- **One cost category** (e.g. hospital costs) reached the HCU threshold among 40% of new HCUs (% of patient in Top 5 categories: Hospital (70.7%); Cancer (8.1%); ODB (7.3%); LTC (5.1%); HC: (3.3%))
- **More than 1 cost category** (e.g. hospital and physician costs) reached the HCU threshold among 13% of HCUs (% of patient in Top 5 categories: Hospital (95.1%); Physician (35.5 %); Rehab (27.8%); CCC (18.6%); HC (13.6%))
- **No single cost category** reached the HCU threshold among 47% of new HCUs (% of patient in Top 5 categories: Physician (99.9%, mean $3022); ODB (99.6%, mean $2127); Hospital (88.7%, mean $5611); Laboratory (87.1%, mean $190); ED (70%, mean $654)

CCC - Continuing Care; ED - Emergency Department; LTC- Long-term care; ODB - Ontario Drug Benefit

Figure 2: Dynamics of change in annual healthcare use, before (baseline) and during incident year, by HCU status and cost categories (mean per patient)

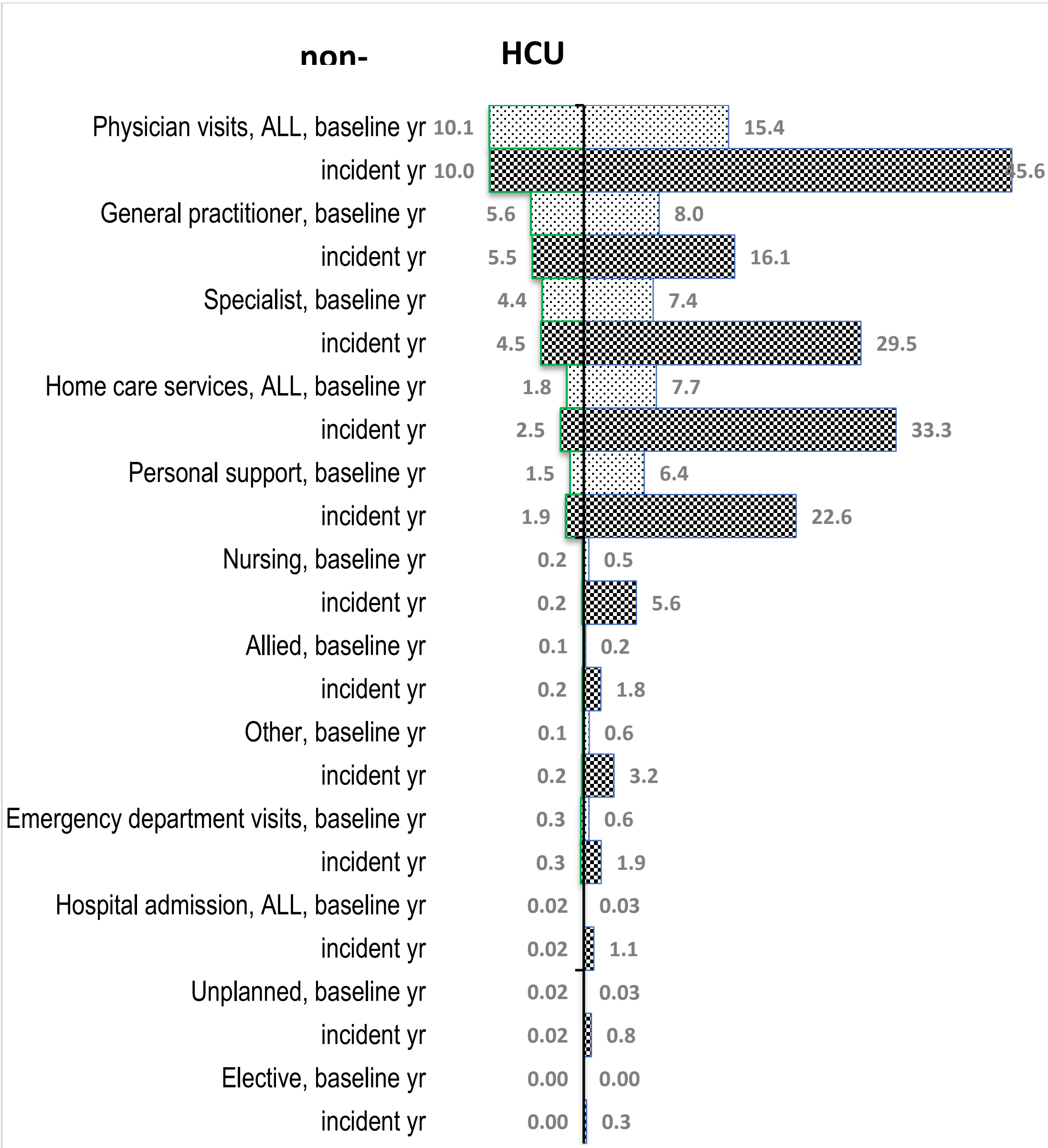
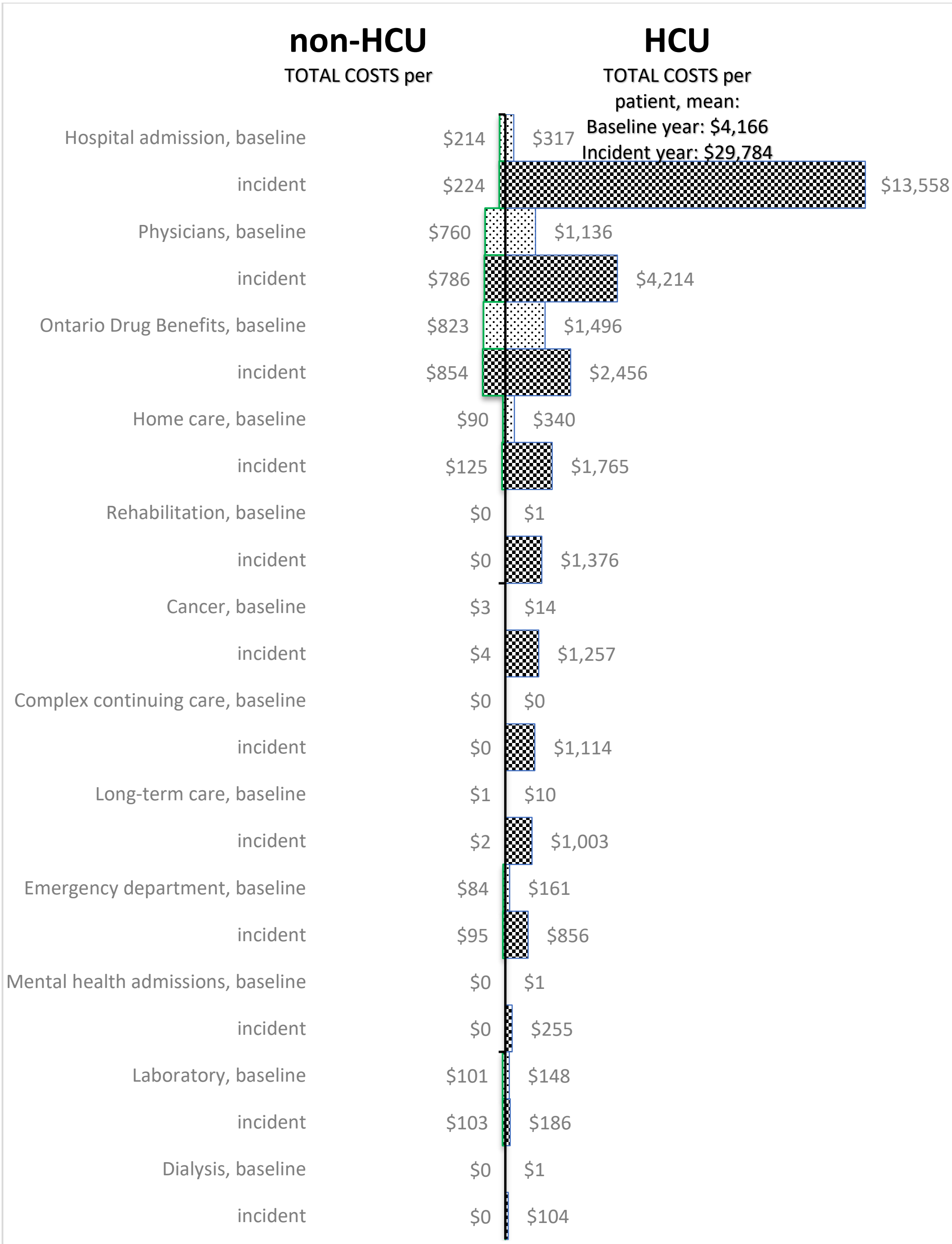
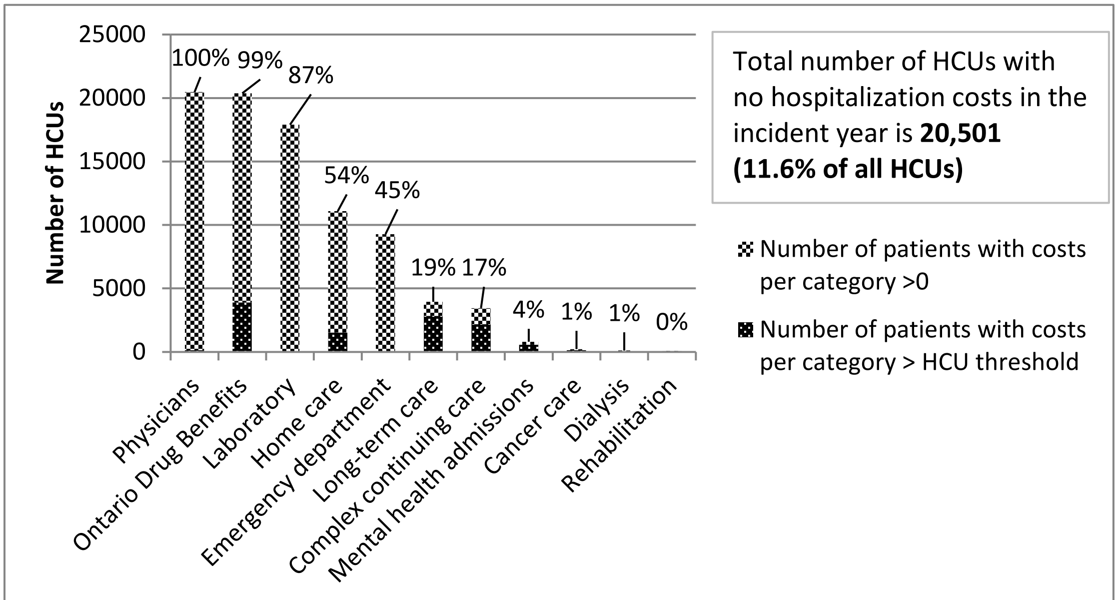


Figure 3: Dynamics of change in annual healthcare care expenditures before and after index year, by HCU status and cost categories (annual, mean per patient)



Appendix 1: HCUs with no hospitalization costs during incident year: contribution of cost categories



Note: The percentages in the figure represent the proportion of patients out of the total number of HCUs without hospitalization expenditures during the incident year that incurred any costs in the corresponding cost category in that year.

Appendix 2: Description of cost components among HCUs and non-HCUs by pre- incident and incident year

Cost components	**FY2012 (pre-incident year)**			**FY2013 (incident year)**		
	HCU N=175847	**Non-HCU N=527541**		**HCU N=175847**	**Non-HCU N=527541**	
	Mean, $ (SD)	**Mean, $ (SD)**	**aSD**	**Mean, $ (SD)**	**Mean, $ (SD)**	**aSD**
Cancer clinics	14 (196)	4 (90)	0.54	1258 (5234)	4 (92)	0.92
Complex continuing care	1 (36)	1 (17)	0.50	1114 (7685)	1 (24)	1.47
Dialysis	2 (40)	1 (15)	0.31	104 (2166)	1 (12)	0.57
Emergency department	162 (327)	84 (226)	0.13	857 (881)	96 (249)	0.62
Home care	341 (1023)	90 (498)	0.28	1765 (3667)	125 (589)	0.29
Hospital admission	318 (864)	215 (714)	0.33	13558 (20529)	225 (743)	0.34
Laboratory	149 (160)	102 (123)	0.07	187 (192)	104 (125)	0.20
Long-term care	11 (192)	1 (45)	0.07	1003 (4800)	3 (91)	0.29
Mental health admissions	1 (60)	1 (33)	0.03	256 (3924)	1 (29)	1.18
Outpatient Drug Benefits	1497 (1441)	824 (1002)	0.01	2456 (3822)	854 (1052)	0.09
Physicians	1136 (821)	761 (671)	0.01	4215 (3217)	787 (694)	0.51
Rehabilitation	1 (41)	1 (33)	0.01	1376 (6792)	1 (20)	0.07
Total cost	**4167 (2664)**	**2372 (2166)**	**0.74**	29785 (29029)	**2471 (2252)**	**1.33**

aSD- absolute standardized difference;
FY- fiscal year

Appendix 3: Description of healthcare use among HCUs and non-HCUs by pre- incident and incident year

Cost components	FY2012 (pre-incident year)			FY2013 (incident year)		
	HCU N=175847	Non-HCU N=527541		HCU N=175847	Non-HCU N=527541	
	Mean (SD)	Mean (SD)	aSD	Mean (SD)	Mean (SD)	aSD
Hospital admission, All	0.04 ± 0.18	0.02 ± 0.14	0.08	1.07 ± 0.87	0.03 ± 0.15	1.68
Elective	0.01 ± 0.07	0.01 ± 0.07	0.01	0.3 ± 0.51	0.01 ± 0.07	0.8
Unplanned	0.03 ± 0.17	0.02 ± 0.13	0.08	0.8 ± 0.89	0.02 ± 0.14	1.24
Emergency department visits	0.56 ± 1.13	0.31 ± 0.8	0.26	1.88 ± 2.2	0.32 ± 0.82	0.94
Physician visits, All	15.43 ± 10.69	10.06 ± 8.9	0.55	45.62 ± 32.55	10.03 ± 8.98	1.49
General practitioner	8.03 ± 6.8	5.64 ± 5.59	0.39	16.08 ± 14.74	5.48 ± 5.56	0.95
Specialist	7.4 ± 6.65	4.43 ± 5.13	0.5	29.55 ± 25.97	4.55 ± 5.24	1.33
Home care services, All	7.74 ± 31.92	1.81 ± 14.15	0.24	33.27 ± 82.17	2.47 ± 17.33	0.52
Personal support	0.54 ± 4.03	0.16 ± 2.00	0.12	5.60 ± 18.59	0.20 ± 2.26	0.41
Nursing	6.44 ± 30.59	1.46 ± 13.53	0.21	22.62 ± 73.93	1.91 ± 16.39	0.39
Allied	0.18 ± 0.99	0.05 ± 0.52	0.17	1.82 ± 4.27	0.15 ± 1.41	0.52
Other	0.58 ± 2.30	0.14 ± 0.96	0.25	3.22 ± 5.23	0.21 ± 1.09	0.8

aSD- absolute standardized difference;
FY- fiscal year

Appendix 4: Regression coefficients, recycled prediction, costs

Care categories / Covariates	Hospital admission			Physician			Homecare			Ontario Drug benefits			Emergency Department			Mental health admission			Total		
	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value
Part 1* p(costs)=0																					
Intercept	1.03	0.04	<.0001	-3.52	0.08	<.0001	9.30	0.05	<.0001	-1.85	0.06	<.0001	3.91	0.03	<.0001	5.94	0.32	<.0001	-4.95	0.09	<.0001
HCU status	-3.79	0.01	<.0001	-5.16	0.15	<.0001	-3.13	0.01	<.0001	-2.25	0.03	<.0001	-2.39	0.01	<.0001	-5.16	0.18	<.0001	-13.88	14.60	0.342
Cost pre	0.00	0.00	<.0001	-0.01	0.00	<.0001	0.00	0.00	<.0001	-0.01	0.00	<.0001	0.00	0.00	<.0001	0.00	0.00	<.0001	-0.01	0.00	<.0001
ADG	-0.09	0.00	<.0001	-0.38	0.00	<.0001	-0.04	0.00	<.0001	-0.34	0.00	<.0001	-0.09	0.00	<.0001	-0.01	0.01	0.214	-0.47	0.01	<.0001
Age	0.02	0.00	<.0001	0.06	0.00	<.0001	-0.08	0.00	<.0001	0.04	0.00	<.0001	-0.02	0.00	<.0001	0.05	0.00	<.0001	0.08	0.00	<.0001
Sex	-0.22	0.01	<.0001	0.13	0.02	<.0001	0.34	0.01	<.0001	0.20	0.01	<.0001	0.04	0.01	<.0001	0.19	0.05	0	0.10	0.02	<.0001
Low income	0.18	0.01	<.0001	0.05	0.02	0.011	-0.06	0.01	<.0001	0.59	0.02	<.0001	-0.03	0.01	<.0001	-0.18	0.06	0.003	0.32	0.02	<.0001
Part 2 p(costs)>0																					
Intercept	6.73	0.02	<.0001	6.26	0.01	<.0001	6.17	0.03	<.0001	5.41	0.01	<.0001	5.46	0.02	<.0001	7.82	0.28	<.0001	6.51	0.01	<.0001
HCU status	2.27	0.00	<.0001	1.53	0.00	<.0001	0.76	0.01	<.0001	0.79	0.00	<.0001	0.88	0.00	<.0001	1.82	0.16	<.0001	2.34	0.00	<.0001
Cost pre	0.00	0.00	<.0001	0.00	0.00	<.0001	0.00	0.00	<.0001	0.00	0.00	<.0001	0.00	0.00	<.0001	0.00	0.00	0.37	0.00	0.00	<.0001
ADG	-0.02	0.00	<.0001	0.03	0.00	<.0001	-0.01	0.00	<.0001	0.02	0.00	<.0001	0.01	0.00	<.0001	-0.02	0.01	<.0001	0.03	0.00	<.0001
Age	0.01	0.00	<.0001	0.00	0.00	<.0001	0.01	0.00	<.0001	0.01	0.00	<.0001	0.01	0.00	<.0001	0.01	0.00	0.002	0.01	0.00	<.0001
Sex	0.08	0.00	<.0001	0.05	0.00	<.0001	0.00	0.01	0.727	0.03	0.00	<.0001	0.02	0.00	<.0001	0.01	0.04	0.882	0.04	0.00	<.0001
Low income	0.02	0.01	0	-0.03	0.00	<.0001	0.00	0.01	0.749	0.09	0.00	<.0001	0.04	0.00	<.0001	0.07	0.05	0.214	0.04	0.00	<.0001
log_theta	0.36	0.00	<.0001	0.79	0.00	<.0001	0.34	0.00	<.0001	0.15	0.00	<.0001	0.84	0.00	<.0001	0.24	0.03	<.0001	0.58	0.00	<.0001

ADG- Aggregate Diagnosis Group; Coeff- regression coefficient; HCU- high-cost user; SE- standard error

Appendix 4: Regression coefficients, recycled prediction, costs (CONT)

Care categories / Covariates	Lab			Dialysis			Cancer care			Long-term care			Continuing complex care			Rehab		
	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value
Part 1 p(costs)=0																		
Intercept	-0.72	0.03	<.0001	7.03	0.33	<.0001	1.96	0.09	<.0001	15.60	0.13	<.0001	15.32	0.23	<.0001	13.08	0.23	<.0001
HCU status	-0.52	0.01	<.0001	-2.14	0.07	<.0001	-3.29	0.02	<.0001	-4.60	0.05	<.0001	-6.87	0.19	<.0001	-7.59	0.21	<.0001
Cost pre	-0.01	0.00	<.0001	-0.03	0.00	<.0001	0.00	0.00	<.0001	0.00	0.00	<.0001	0.00	0.00	<.0001	0.00	0.00	<.0001
ADG	-0.15	0.00	<.0001	-0.04	0.01	<.0001	0.01	0.00	0	0.03	0.00	<.0001	0.04	0.00	<.0001	0.02	0.00	<.0001
Age	0.02	0.00	<.0001	0.02	0.00	<.0001	0.05	0.00	<.0001	-0.11	0.00	<.0001	-0.07	0.00	<.0001	-0.04	0.00	<.0001
Sex	0.05	0.01	<.0001	-0.60	0.06	<.0001	-0.11	0.02	<.0001	0.42	0.02	<.0001	0.13	0.02	<.0001	0.26	0.02	<.0001
Low income	0.08	0.01	<.0001	-0.39	0.07	<.0001	0.22	0.02	<.0001	-0.11	0.02	<.0001	-0.01	0.03	0.763	0.02	0.02	0.364
Part 2 p(costs)>0																		
Intercept	4.41	0.01	<.0001	6.22	0.44	<.0001	8.30	0.10	<.0001	7.54	0.10	<.0001	7.15	0.23	<.0001	7.54	0.19	<.0001
HCU status	0.30	0.00	<.0001	3.99	0.08	<.0001	2.76	0.02	<.0001	1.81	0.04	<.0001	2.47	0.19	<.0001	1.74	0.18	<.0001
Cost pre	0.00	0.00	<.0001	0.00	0.00	0.792	0.00	0.00	<.0001	0.00	0.00	<.0001	0.00	0.00	0	0.00	0.00	0.486
ADG	0.01	0.00	<.0001	-0.05	0.01	<.0001	-0.01	0.00	<.0001	-0.01	0.00	<.0001	-0.01	0.00	0.05	0.00	0.00	0.143
Age	0.00	0.00	<.0001	0.00	0.01	0.958	-0.02	0.00	<.0001	0.01	0.00	<.0001	0.01	0.00	<.0001	0.01	0.00	<.0001
Sex	0.02	0.00	<.0001	-0.04	0.07	0.547	0.12	0.02	<.0001	-0.06	0.02	0.001	-0.01	0.02	0.665	0.10	0.02	<.0001
Low income	0.03	0.00	<.0001	-0.33	0.08	<.0001	-0.07	0.02	0.003	-0.02	0.02	0.174	0.01	0.03	0.652	0.02	0.02	0.228
log_theta	0.81	0.00	<.0001	-0.68	0.03	<.0001	-0.07	0.01	<.0001	0.35	0.01	<.0001	0.02	0.01	0.176	0.44	0.01	<.0001

ADG- Aggregate Diagnosis Group; Coeff- regression coefficient; HCU- high-cost user; SE- standard error

*Two-part models (Hurdle regression) were specified to manage zero values in the response variables: Part 1 used a logistic regression to predict the probability of positive values of the outcome; Part 2 specified a gamma model was applied for positive costs

Appendix 5: Regression coefficients, recycled prediction, health care use

Care categories / Covariates	Hospital admission, All			Hospital admission, urgent			Hospital admission, elective			Physician visits, All			Physician visits, Specialists			Physician visits, General practitioner		
	Coeff	**SE**	**P-value**	**Coeff**	**SE**	**P-value**	**Coeff**	**SE**	**P-value**	**Coeff**	**SE**	**P-value**	**Coeff**	**SE**	**P-value**	**Coeff**	**SE**	**P-value**
Part 1* p(event) ≠0																		
Intercept	0.57	0.05	<.0001	-8.08	0.05	<.0001	4.07	0.06	<.0001	7.74	0.15	<.0001	4.80	0.05	<.0001	4.03	0.06	<.0001
HCU status	5.11	0.01	<.0001	4.48	0.01	<.0001	4.66	0.02	<.0001	5.60	0.14	<.0001	3.78	0.03	<.0001	2.71	0.03	<.0001
Pre-incident value	0.78	0.03	<.0001	0.82	0.03	<.0001	0.80	0.07	<.0001	0.40	0.00	<.0001	0.29	0.00	<.0001	0.62	0.00	<.0001
Age	0.01	0.00	<.0001	0.05	0.00	<.0001	-0.07	0.00	<.0001	-0.05	0.00	<.0001	-0.03	0.00	<.0001	-0.04	0.00	<.0001
ADG	0.00	0.00	0.002	0.00	0.00	<.0001	0.00	0.00	0.006	0.38	0.00	<.0001	0.25	0.00	<.0001	0.26	0.00	<.0001
Sex	0.08	0.01	<.0001	0.12	0.01	<.0001	0.05	0.01	<.0001	-0.13	0.01	<.0001	-0.12	0.01	<.0001	-0.12	0.01	<.0001
Low income	-0.04	0.01	6E-04	0.17	0.01	<.0001	-0.40	0.02	<.0001	-0.20	0.02	<.0001	-0.20	0.01	<.0001	-0.16	0.01	<.0001
Part 2 p(event) ≠0																		
Intercept	-2.16	0.07	<.0001	-6.77	0.19	<.0001	-1.37	0.20	<.0001	3.02	0.01	<.0001	3.10	0.01	<.0001	1.41	0.01	<.0001
HCU status	4.21	0.13	<.0001	4.62	0.17	<.0001	2.59	0.28	<.0001	1.33	0.00	<.0001	1.63	0.00	<.0001	0.91	0.00	<.0001
Pre-incident value	0.39	0.03	<.0001	0.42	0.03	<.0001	0.71	0.11	<.0001	0.03	0.00	<.0001	0.04	0.00	<.0001	0.06	0.00	<.0001
Age	0.01	0.00	<.0001	0.01	0.00	<.0001	-0.01	0.00	0.041	0.00	0.00	<.0001	0.00	0.00	<.0001	0.01	0.00	<.0001
ADG	0.02	0.00	<.0001	0.03	0.00	<.0001	0.00	0.00	0.268	0.02	0.00	<.0001	0.02	0.00	<.0001	0.02	0.00	<.0001
Sex	0.19	0.01	<.0001	0.11	0.01	<.0001	0.29	0.03	<.0001	0.02	0.00	<.0001	0.06	0.00	<.0001	-0.01	0.00	<.0001
Low income	0.07	0.01	<.0001	0.06	0.02	0.0004	-0.04	0.05	0.45	0.01	0.00	<.0001	-0.02	0.00	<.0001	0.05	0.00	<.0001
Scale parameter	1.51	0.08		0.60	0.04	<.0001	0.00	0.00		0.32	0.00		0.49	0.00		0.36	0.00	

ADG- Aggregate Diagnosis Group; Coeff- regression coefficient; HCU- high-cost user; SE- standard error

Appendix 5: Regression coefficients, recycled prediction, health care use (CONT)

Care categories / Covariates	Emergency department visits			Home care services, All**			Home care services, Personal support			Home care services, Nursing			Home care services, Allied			Home care services, Other**		
	Coeff	**SE**	**P-value**	**Coeff**	**SE**	**P-value**	**Coeff**	**SE**	**P-value**	**Coeff**	**SE**	**P-value**	**Coeff**	**SE**	**P-value**	**Coeff**	**SE**	**P-value**
Part 1 p(event) ≠0																		
Intercept	-1.58	0.03	<.0001	-9.51	0.05	<.0001	-9.22	0.07	<.0001	-3.04	0.05	<.0001	-7.21	0.05	<.0001	-9.28	0.05	<.0001
HCU status	2.40	0.01	<.0001	3.11	0.01	<.0001	2.97	0.01	<.0001	3.06	0.01	<.0001	2.71	0.01	<.0001	3.07	0.01	<.0001
Pre-incident value	0.39	0.00	<.0001	0.08	0.00	<.0001	0.09	0.00	<.0001	0.11	0.00	<.0001	0.26	0.00	<.0001	0.58	0.00	<.0001
Age	0.02	0.00	<.0001	0.08	0.00	<.0001	0.09	0.00	<.0001	0.02	0.00	<.0001	0.07	0.00	<.0001	0.08	0.00	<.0001
ADG	0.09	0.00	<.0001	0.05	0.00	<.0001	0.02	0.00	<.0001	0.02	0.00	<.0001	0.04	0.00	<.0001	0.05	0.00	<.0001
Sex	0.04	0.01	<.0001	-0.34	0.01	<.0001	-0.47	0.01	<.0001	0.12	0.01	<.0001	-0.45	0.01	<.0001	-0.34	0.01	<.0001
Low income	0.04	0.01	<.0001	0.04	0.01	<.0001	0.15	0.01	<.0001	-0.10	0.01	<.0001	-0.01	0.01	0.600	0.08	0.01	<.0001
Part 2 p(event) ≠0																		
Intercept	-0.02	0.03	0.658	0.52	0.00	<.0001	-0.70	0.14	<.0001	2.40	0.06	<.0001	0.20	0.05	<.0001	-0.47	0.01	<.0001
HCU status	0.97	0.01	<.0001	0.74	0.00	<.0001	0.62	0.03	<.0001	0.76	0.02	<.0001	0.24	0.01	<.0001	0.74	0.00	<.0001
Pre-incident value	0.21	0.00	<.0001	0.01	0.00	<.0001	0.01	0.00	<.0001	0.03	0.00	<.0001	0.02	0.00	<.0001	0.03	0.00	<.0001
Age	0.00	0.00	0.179	0.03	0.00	<.0001	0.02	0.00	<.0001	0.00	0.00	<.0001	0.01	0.00	<.0001	0.02	0.00	<.0001
ADG	0.03	0.00	<.0001	0.00	0.00	<.0001	-0.01	0.00	0.001	0.00	0.00	0.091	0.02	0.00	<.0001	0.00	0.00	<.0001
Sex	0.09	0.01	<.0001	-0.13	0.00	<.0001	-0.07	0.02	0.006	-0.03	0.01	0.011	-0.11	0.01	<.0001	0.00	0.00	0.3217
Low income	0.02	0.01	0.005	0.05	0.00	<.0001	-0.06	0.03	0.026	0.03	0.02	0.061	-0.14	0.01	<.0001	0.04	0.00	<.0001
Scale parameter	1.09	0.02					115.73	0.00		2.12	0.02		1.01	0.01				

ADG- Aggregate Diagnosis Group; Coeff- regression coefficient; HCU- high-cost user; SE- standard error
*For count data, two-part models were applied to manage zero values in the response variables: Part 1 used a logistic regression to predict the probability of positive values of the outcome; Part 2 was a negative binomial or Poisson model for positive counts,
**-models were fit using Poisson distribution

Chapter 4

Muratov *et al. BMC Geriatrics* (2018) 18:262
https://doi.org/10.1186/s12877-018-0952-7

BMC Geriatrics

RESEARCH ARTICLE Open Access

Regional variation in healthcare spending and mortality among senior high-cost healthcare users in Ontario, Canada: a retrospective matched cohort study

Sergei Muratov[1,2*], Justin Lee[1,3,4,5], Anne Holbrook[1,4], Andrew Costa[1,6,7], J. Michael Paterson[6,11], Jason R. Guertin[8,9], Lawrence Mbuagbaw[1,10], Tara Gomes[6,12,13], Wayne Khuu[6] and Jean-Eric Tarride[1,2,7]

Abstract

Background: Senior high cost health care users (HCU) are a priority for many governments. Little research has addressed regional variation of HCU incidence and outcomes, especially among incident HCU. This study describes the regional variation in healthcare costs and mortality across Ontario's health planning districts [Local Health Integration Networks (LHIN)] among senior incident HCU and non-HCU and explores the relationship between healthcare spending and mortality.

Methods: We conducted a retrospective population-based matched cohort study of incident senior HCU defined as Ontarians aged ≥66 years in the top 5% most costly healthcare users in fiscal year (FY) 2013. We matched HCU to non-HCU (1:3) based on age, sex and LHIN. Primary outcomes were LHIN-based variation in costs (total and 12 cost components) and mortality during FY2013 as measured by variance estimates derived from multi-level models. Outcomes were risk-adjusted for age, sex, ADGs, and low-income status. In a cost-mortality analysis by LHIN, risk-adjusted random effects for total costs and mortality were graphically presented together in a cost-mortality plane to identify low and high performers.

Results: We studied 175,847 incident HCU and 527,541 matched non-HCU. On average, 94 out of 1000 seniors per LHIN were HCU (CV = 4.6%). The mean total costs for HCU in FY2013 were 12 times higher that of non-HCU ($29,779 vs. $2472 respectively), whereas all-cause mortality was 13.6 times greater (103.9 vs. 7.5 per 1000 seniors).
Regional variation in costs and mortality was lower in senior HCU compared with non-HCU. We identified greater variability in accessing the healthcare system, but, once the patient entered the system, variation in costs was low. The traditional drivers of costs and mortality that we adjusted for played little role in driving the observed variation in HCUs' outcomes. We identified LHINs that had high mortality rates despite elevated healthcare expenditures and those that achieved lower mortality at lower costs. Some LHINs achieved low mortality at excessively high costs.

Conclusions: Risk-adjusted allocation of healthcare resources to seniors in Ontario is overall similar across health districts, more so for HCU than non-HCU. Identified important variation in the cost-mortality relationship across LHINs needs to be further explored.

Keywords: Senior high-cost users, Small area variation, Healthcare expenditures, Mortality

* Correspondence: muratos@mcmaster.ca
[1]Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada
[2]Programs for Assessment of Technology in Health (PATH), The Research Institute of St. Joe's Hamilton, St. Joseph's Healthcare, Hamilton, ON, Canada
Full list of author information is available at the end of the article

Background

High-cost health care users (HCU), a minority of individuals who consume a large proportion of health care resources, are a diverse group [1]. Due to their high burden on the healthcare system, a better understanding of various segments of the HCU population is needed to develop evidence-informed health care policy [1, 2]. In particular, seniors (patients 65 years of age and older), who account for about 15% of the population in the province of Ontario, account for approximately 60% of the total costs incurred by all HCU in the province [3–5]. Further, nearly half of senior HCU each year are incident cases [6, 7]. These "new" cases represent a stratum of the HCU population that can potentially be a target of preventative interventions and management, but they have not been adequately studied, especially in the context of regional variation.

Large geographical disparities in health care services have been documented globally [8, 9]. In Canada, marked regional variation has been identified in key healthcare services such as hospitalization [10], surgical procedures [11, 12], and use of prescription drugs [13, 14]. In contrast to this evidence of disparities in individual healthcare services, there is little information on variation in healthcare spending in the Canadian provincial context. While reports on regional variation in healthcare spending, especially the Medicare costs, have dominated the US political debate for more than a decade [15–19], only one Canadian study (British Columbia[BC]) has investigated regional variation in healthcare expenditures and found it to be modest [20]. While very informative, the BC study was not intended to investigate seniors specifically, not to mention senior HCU. Moreover, except for the total healthcare spending, the BC study did not provide information on variation among individual cost components such as hospitalization and physician costs which limits our understanding of the processes of care that contribute to higher or lower variation [21].

Understanding regional variation in health services utilization, costs and health outcomes can inform health services planning for senior patients, including senior HCU, in several ways. First, it allows planners to explore potential drivers of variation that deserve attention by describing the distribution of patient and care characteristics across health districts [22, 23]. Second, evidence suggests that planning and implementing health services with an "equity lens" can improve equity in resources allocation [24] and healthcare services use [25–27], and reduce regional variation in outcome distribution [28]. Third, measuring the relationship between costs and health outcomes among health regions is critical for policy makers to identify geographical "pockets" of efficient care (areas with lower spending and better outcomes). Recent studies have reported the level of inefficiency in Canada at 20% [29] with significant variations across Canadian provinces [30]. Moreover, even though available evidence of healthcare regional variation and efficiency has led policy makers to entertain the idea of cutting reimbursement rates in higher-spending regions [15, 31] or to establish new provider-physician integrated entities with spending benchmarks (accountable care organizations) [32], there is still a gap in our knowledge as to how regional disparities in healthcare spending affect regional patterns of health outcomes [33]. The lack of evidence on geographical variation in health outcomes seems to have contributed to the gap [34, 35].

To better inform decision and policy making in Ontario and fill a gap in the literature, the objectives of this study were: 1) to estimate regional variation in healthcare costs (total and by cost categories) and mortality among incident senior HCU compared to senior non-HCU; and 2) to examine the relationship between health spending and mortality by health districts for senior incident HCU compared to senior non-HCU.

Methods

Study design

A retrospective population-based matched cohort study was conducted using province-wide linked administrative data. More details on the study population and data sources are published elsewhere but are briefly summarized below [36].

Study population

We generated a cohort of all incident senior HCU in the province of Ontario. This cohort was defined as consisting of seniors (aged ≥66 years) with annual total healthcare expenditures within the top 5% threshold of all Ontarians in the 2013 Ontario government fiscal year (FY2013) (i.e. incident year), and not in the top 5% in the 2012 fiscal year (FY2012).The threshold of 5% to define HCU is aligned with previous Canadian studies of this population [3, 7, 37, 38].The incident HCU cohort was matched to a cohort of non-HCU using a 1:3 matching ratio, without replacement based on age at cohort entry (+/− 1 month), sex and residence (based on Local Health Integration Networks [LHIN]). The "non-HCU" cohort was defined as those whose annual total health care expenditures in the 2012 and 2013 fiscal years were both below the financial threshold of the top 5% of all Ontarians in the respective year.

Data sources

The patient-level dataset was created using 19 health administrative databases [36]. These datasets were linked using unique encoded identifiers and analyzed at the Institute for Clinical Evaluative Sciences (ICES) [39]. Health care expenditures were calculated using a person-level health utilization costing algorithm [40]. Total healthcare expenditures were comprised of 12 separate health service cost categories. Hospital costs were the sum of costs associated with inpatient care and same-day surgery. Physician costs were the sum of fee-for-service billings and capitation payments. Costs reported in this study are based on patients' geographic location of residence. Costs are expressed in 2013 Canadian Dollars.

Geographic unit of analysis

We used LHINs, Ontario's regional health districts, as the geographic unit of analysis. Ontario's 14 LHINs are responsible for the funding, planning and management of hospital- and community-based health services delivered to all residents within their geographic boundaries [41]. Services covered by the LHINs include most of hospital and community care such as inpatient care, long-term and home care, community mental health, rehabilitation and hospices among others [42], but exclude physician services, which are funded from a separate envelope.

Variables

The study population was described at baseline (i.e., the year before HCU incident status), including comparisons of socio-demographic determinants (age, sex, residence, low income), health status (degree of morbidity, proportion of chronic conditions) and health system factors (e.g., number of physicians in the circle of care and whether a geriatrician was visited) between HCU and matched non-HCU. Subjects with low income status were identified based upon net household income reported to receive public drug benefit subsidy in FY2012. Compared to census-based neighborhood income measures, the Ontario Drug Benefit (ODB)-based low income status is a better reflection of personal income, as it relies upon actual net income. For a small proportion of HCU (3%) and non-HCU (13%) who did not fill a prescription in FY2012, low-income status was defined as census neighborhood income quintile 1. Rurality was defined using the Rural Index of Ontario (RIO): an ordinal measure ranging from 0 (urban) to 100 (rural) that considers population density and travel time to the nearest health facility [43].

Several measures were employed to describe health status. Level of morbidity was measured using Johns Hopkins Aggregated Diagnosis Groups (ADGs) that are derived from Johns Hopkins Adjusted Clinical Groups (ACGs): a person-focused, diagnosis-based way to measure patients' illness [44]. In addition, the proportions of patients with prior malignancy and mental health conditions were computed using John Hopkins Expanded Diagnosis Clusters (EDCs). Finally, the proportions of patients with chronic obstructive pulmonary disease, congestive heart failure, diabetes, and rheumatoid arthritis were estimated using ICES-derived, validated chronic disease cohorts [45, 46].

Outcomes

Several outcomes were assessed. HCU rate for each LHIN was defined as the number of senior HCU over the total number of seniors residing in the LHIN per 1000 population. Mean per capita total healthcare expenditures and mean per capita health expenditures for each care category were calculated as the costs incurred in the incident year over the total population in the HCU and non-HCU cohort. Finally, mortality for each cohort was defined as the prevalence of all-cause death within the incident year.

Statistical analysis

Descriptive statistics (counts [%]; mean [SD] or median [Q1, Q3]) were summarized for baseline individual characteristics and outcomes. Characteristics of subjects in both HCU and non-HCU cohorts were compared using absolute standardized differences (SDD). SDDs of more than 0.1 are considered to indicate meaningful differences between the cohorts [47]. To describe the variation between the LHINs in terms of costs and outcomes, the coefficient of variations (CVs) defined as the ratio of the standard deviation to the mean were determined.

Because the calculated intra-class correlation coefficient (ICC) pointed toward statistically significant clustering within the LHINs across most of the cost components and mortality in both cohorts (Additional file 1), we fitted a mixed effects model to estimate between-region variation and risk-adjust for age, sex, the number of ADGs per patient, and low-income status for both costs and mortality. Compared to the CV or other summary statistics characterizing regional variation, these models provide additional information, including the between-LHIN variance estimate and the proportion of the observed variation explained by patient characteristics.

We specified the following general equation (Additional file 2):

$$y_{ij} = \left(\mathrm{Beta}_0 + u_{0j}\right) + \sum \mathrm{Beta}_{ij^*} X_{ij} + e_{ij};$$

where yij – the outcome (costs or mortality) in patient i from LHIN_j; $Beta_0$ - the provincial mean; $u0j$ – the random effect for each LHIN that is assumed $u0j \sim N(0, \sigma 2u)$; $Beta_{ij}$ - the fixed effects of individual level characteristics; Xij - the vector of covariates at the individual level; eij - the residual error.

This type of models assumes that the mean outcome value for each LHIN vary randomly according to a normal distribution ($u0j \sim N(0, \sigma 2u)$) whereas the effect of the patients' covariates is fixed among the LHINs. The main interest in this type of analyses is the random effect ($u0j$) which characterizes variation between LHINs, where $\sigma 2u$ is the direct estimate of the variance.

For the mortality analyses, logistic regression was conducted by fitting generalized linear mixed models (GLMM) according to the general model specification provided above. To model healthcare expenditures, two methods were used based on the proportion of zero costs values in the data. Zero cost values arise when healthcare resources are not consumed (e.g. no contact with healthcare system or no hospitalization). For healthcare categories with no zero costs values GLMM were used. In the presence of zero costs values in the data, Hurdle mixed models were used to account for zeros [48, 49]. Hurdle models, also referred to as a two-part model, assumes that costs are generated by two statistically different processes. A binomial distribution (part 1) was used to determine whether any costs were incurred, and a gamma distribution (part 2) was employed to model positive costs (instances when costs> 0) [49–51]. Expected costs resulting from Hurdle models are then calculated by multiplying the probability of observing a cost by the value of the costs when observed. LHIN-specific random effects were incorporated into each part of the model to estimate between-LHIN variation in the probability of incurring any costs ($\sigma 2u1$) and variation in costs once they were incurred ($\sigma 2u2$), resulting into two random effects values. Similarly, the fixed effects associated with the individual level characteristics were included in each part of the Hurdle model.

Unadjusted and risk adjusted models were compared using both the likelihood ratio test (LRT) that follows a chi-squared distribution (p-value has to be less than 0.05) and information criteria (e.g., Akaike and Bayesian: lower values equal better fit) [52–54]. Statistical significance of coefficients was considered at alpha = 0.05. We also compared the observed data with predicted values by LHIN to investigate model adequacy. The coefficient of determination R^2 was calculated to measure the proportion of the observed regional variation in outcomes explained by the covariate for each model (please see Additional file 2) [55, 56]. To assess uncertainty around the estimates of the random effects, we generated a bootstrap 95% confidence interval (CI) from the bootstrap sample of 1000 by looking at the 2.5th and 97.5th percentiles in this distribution.

To determine whether certain regions are more efficient than others, we examined the relationship between total healthcare spending (positive costs) and mortality in both cohorts. Building on an approach previously employed for hospital profiling [57, 58], the risk-adjusted random effects for total costs and mortality were first ordered from the smallest to the largest and then graphically presented together in a cost-mortality plane, one for each cohort. LHINs located at the left bottom quadrant of the plots (where the X axis represents mortality and the Y axis costs) are more efficient than others provided that the CI of random effects for both total costs and mortality does not cross 0. Analyses were conducted using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA). The NLMIXED procedure was used to fit all the models. To visualize HCU rates between LHINs, a heat map was created using QGIS (Quantum geographic information system, https://qgis.org).

Results

Baseline characteristics

We included 703,388 subjects (HCU = 175,847, non--HCU = 527,541). The HCU were similar to non-HCU with respect to age, sex, the proportion residing in urban centres, and the number of low-income subjects (Table 1). However, compared to non-HCU, HCU tended to have a higher number of comorbidities, and a larger proportion of subjects with a malignancy, common chronic diseases, and mental health issues. HCU were dispensed a higher number of prescription drugs, had more physicians involved in their circle of care, and were seen by a geriatrician more often. Additional file 3 provides more information on the variation in these characteristics between the 14 LHINs.

HCU rate

Figure 1 shows the distribution of HCU among the 14 health regions. The size of LHINs' senior HCU population ranged from a low of 88.1 per 1000 seniors (Central 08

Table 1 Patient baseline individual and care characteristics, pre-incident year

Characteristic	HCU Mean (SD)	Non-HCU Mean (SD)	SDD
Age: subgroup (%)			
66–74	39.7 (2.5)	39.7 (2.5)	0.00
75–84	39.9 (0.8)	39.9 (0.8)	0.00
≥ 85	20.5 (2.5)	20.5 (2.5)	0.00
Sex (F, %)	52.7 (1.3)	52.7 (1.3)	0.00
Rurality (urban, %)	61.8 (27.6)	62.7 (28.0)	0.03
Low income senior (%)	17.6 (5.2)	16.8 (5.7)	0.01
Number of ADGs (mean)	10.1 (0.4)	7.9 (0.3)	0.50
Malignant neoplasms (%)	32.2 (2.6)	23.4 (3.2)	0.20
Common chronic conditions* (%)	60.6 (2.4)	44.8 (2.3)	0.30
Mental health# (%)	37.6 (4.1)	26.9 (2.5)	0.20
Number of MDs involved in care (mean)	8.1 (0.5)	5.6 (0.3)	0.50
Seen by a geriatrician (%)	2.8 (1.3)	1.1 (0.5)	0.12
Number of prescription drugs (mean)	8.4 (0.4)	5.6 (0.3)	0.60
Acute inpatient care (%)	3.8 (1.1)	2.1 (0.7)	0.10

ADGs- Aggregated Diagnosis Groups; HCU- high-cost user; *ICES- derived common chronic conditions (either one of the following: CHF-congestive heart failure; COPD- chronic obstructive pulmonary disease; DM- diabetes, MI- myocardial infarction, RA- rheumatoid arthritis); LHIN – Local Health Integrated Network; SD- Standard Deviation; # includes any of mental health conditions among Expanded Diagnosis Clusters (PSY01–12); SDD – absolute standardized difference; SDD ≥ 0.1 indicates a meaningful difference

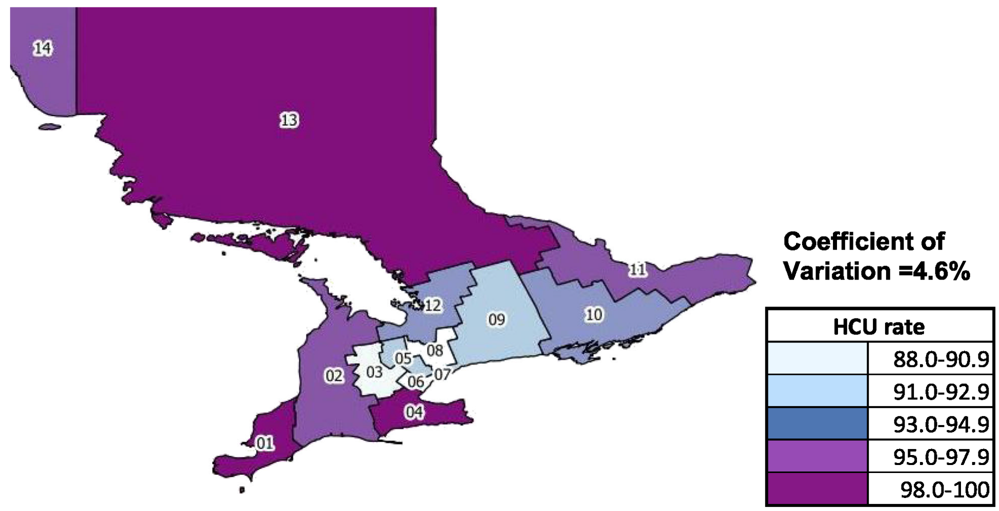


Fig. 1 HCU rate, per 1000 seniors. 01- Erie St. Clair; 02- South West; 03- Waterloo Wellington; 04- Hamilton Niagara Haldimand Brant; 05- Central West; 06- Mississauga Halton; 07- Toronto Central; 08- Central; 09- Central East; 10- South East; 11- Champlain; 12- North Simcoe Muskoka; 13- North East; 14- North West

LHIN) to a high of 100.2 per 1000 seniors (North East 13 LHIN).One of the northernmost regions of Ontario (North East 13 LHIN), and two health regions in the southwest of the province (Erie St. Clair 01 LHIN and Hamilton 04 LHIN) had the highest rates of HCU in the province, whereas health regions in close proximity to Toronto tended to exhibit the lowest rates. Overall variation in HCU rates across the province had a CV of 4.6%.

Unadjusted and adjusted costs and mortality by LHIN

The mean total 1-year observed costs per individual were $29,646 CAD and $2452 CAD for HCU and non-HCU, respectively. Hospital admissions represented the largest cost component among incident HCU accounting for 48.2% of the total costs. In non-HCU, prescription drugs were closely followed by physician costs as the top contributors to the total expenditures at 38.9% and 35.8%, respectively, while hospitalization accounted for 10.2%. All-cause mortality during the incident year among HCU was 13.6 times greater that of non-HCU (104.2 vs. 7.7 per 1000 seniors, respectively). Additional file 4 presents the observed and adjusted mortality and costs (total healthcare expenditures and its components) as well as the associated CVs. As shown in the tables, there was a very good agreement between observed and adjusted mean values across the mortality and cost components in both cohorts suggesting a good fit of the data. CVs for total costs and mortality were 3% and 6.8% for the HCU cohort, indicating little variation between LHINs. Higher CV values were observed for several cost components such as complex continuing care (CV of 45.1%), rehabilitation (CV of 7.2%), and dialysis (CV of 36.2%), and CVs were higher for the non-HCU matched cohort. In all analyses that converged, the models incorporating patient individual covariates were preferred to the models without covariates as shown by the LRT tests and lower AIC and BIC values. For non-HCU, the two-part mixed effects models did not converge in 4 cost components (mental health, long-term care, complex continuing care, rehabilitation services) due to very low number of patients that incur these costs.

Between-LHIN variation in mortality and costs

Starting with mortality, the results of the mixed models indicate that the LHIN-specific variation in mortality (represented by the variance $\sigma 2u$) was statistically significant and was 10 times as low compared to non-HCU (Table 2). All covariates were statically significant with the expected signs although the impact of the number of ADG was different for HCU and non-HCU. As shown by the values of the coefficient of determination R^2, approximately 9% the observed variation in mortality among HCU is explained by patients' characteristics while this percentage is 18% for non-HCU.

Table 3 presents regression results for total costs among HCU and non-HCU. Since all the HCU had a contact with the healthcare system and incurred a cost, we used a GLMM to fit the data for the HCU. Results indicated that the LHIN-specific variation was small but

Table 2 Regression results: mortality (adjusted, log scale)

Mortality		
Variables	HCU#	Non-HCU#
	Coefficient (SE)	Coefficient (SE)
Variance in mortality, σ2u	0.005 (0.003)*	0.051 (0.021)*
Intercept	−7.154 (0.087)*	−13.883 (0.201)*
Age	0.071 (0.002)*	0.109 (0.003)*
Sex, M	0.346 (0.017)*	0.392 (0.033)*
ADG	−0.04 (0.002)*	0.052 (0.004)*
Low income status	0.091 (0.02)*	0.227 (0.039)*
R^2, %	8.8%	17.9%
LRT (Chi2 dist, $p < 0.05$)	5207.2	2800.21

- Estimated through a mixed effects two-part model; * - estimates were statistically significant at $p < .05$; ADGs- Aggregated Diagnosis Groups; HCU- high-cost user; LHIN – Local Health Integrated Network; LRT- likelihood ratio test; R^2- coefficients of determination; SE- Standard Error

Table 3 Regression results: total public healthcare expenditures (adjusted, log scale)

Total costs		
Variables	HCU#	Non-HCU&
	Coefficient (SE)	Coefficient (SE)
Variance in probability of incurring costs, σ2u1		0.065 (0.026)*
Variance in costs once incurred, σ2u2	0.0009 (0.0004)*	0.001 (0.001)*
Covariance between σ2u1 and σ2u2		0.006 (0.003)
Probability (costs≠0)		
Intercept		4.49 (0.16)*
Age		−0.067 (0.002)*
Sex, M		− 0.205 (0.03)*
ADG		1.018 (0.009)*
Low income status		−0.129 (0.035)*
Costs > 0		
Intercept	9.74 (0.02)*	5.946 (0.025)*
Age	0.008 (0.0002)*	0.016 (0.001)*
Sex, M	0.064 (0.003)*	0.044 (0.005)*
ADG	−0.011 (0.0004)*	0.081 (0.001)*
Low income status	0.018 (0.004)*	0.134 (0.006)*
log_theta	0.788 (0.003)*	0.473 (0.004)*
R^2 (part 1), %		87.0%
R^2 (part 2), %	1.6%	19.7%
LRT (Chi2 dist, $p < 0.05$)	2333.0	88,500.57

& - Estimated through GLMM; # - Estimated through a mixed effects two-part model; * - estimates were statistically significant at $p < .05$; ADGs- Aggregated Diagnosis Groups; HCU- high-cost user; LHIN – Local Health Integrated Network; Log-theta- the logarithm of the shape parameter of gamma distribution; LRT- likelihood ratio test; R^2- coefficients of determination; SE- Standard Error

statistically significant ($\sigma 2u2$). All covariates were statistically significant too but only 1.6% (i.e. R^2) of the observed regional variation in total costs of senior HCU was due to patient characteristics. Because 9.4% of non-HCU incurred no costs at all, we fitted a mixed effects two-part model to the non-HCU total cost data. Since two distributions generate the data, the model generates two random-effects to estimate between-LHIN variation in the probability of incurring any costs ($\sigma 2u1$) and variation in costs once they were incurred ($\sigma 2u2$). As shown in this table, the variation ($\sigma 2u1$) among HCU in system contacts overall was 65 times as high as $\sigma 2u2$, both estimates statistically significant. All covariates were statistically significant in explaining each part of the model. The values of R^2 for the non-HCU cohort indicated that 87% of the LHIN variation related to the probability of incurring a cost was explained by the covariates while only 19.7% of the variation once a cost was incurred was explained by patient characteristics of non-HCU.

In addition to the total costs, Additional file 5A-B presents variance estimates across the cost components in both cohorts ($\sigma 2u1$, where available, and $\sigma 2u2$, log-scale). With the exception of the analysis of costs associated with physician visits, all cost components were analysed with two-part models. Overall, variation in incurred expenditures across cost components was higher compared with that of the total costs. Similarly, variation in the probability of positive costs was substantially greater. LHIN-specific variation in dialysis costs (both part 1 and part 2 of the model) had the highest significant values in HCU, whereas regional variation in cancer expenditures was an outlier among non-HCU. The covariates traditionally representing health care needs explained much of the observed variation in the probability of accessing healthcare: R^2 for part 1 of the models ranged from 0.5 to 34.5% (HCU) and 6.8% to 87.0%(non-HCU). In contrast, once the costs were incurred, the role of these covariates greatly diminishes. R^2 for part 2 ranged from 0.3 to 5.1% (HCU) and 2.7% to 19.7% (non-HCU).

Cost-mortality relationship

To identify LHINs that are more efficient than others (e.g. lower spending and mortality), LHINs were ranked by random effects for total costs and mortality (Figs. 2 and 3). As shown in Figs. 2a–c presenting the random effects for each LHIN and the associated 95% CIs among HCU, there were several LHINs in which the random effects were statistically significant for mortality (Fig. 2a) and costs (Fig. 2b). When costs and mortality were combined in a cost-mortality plane (Fig. 2c), only LHINs 1, 3, 4 and 7 had the random effects significant for both

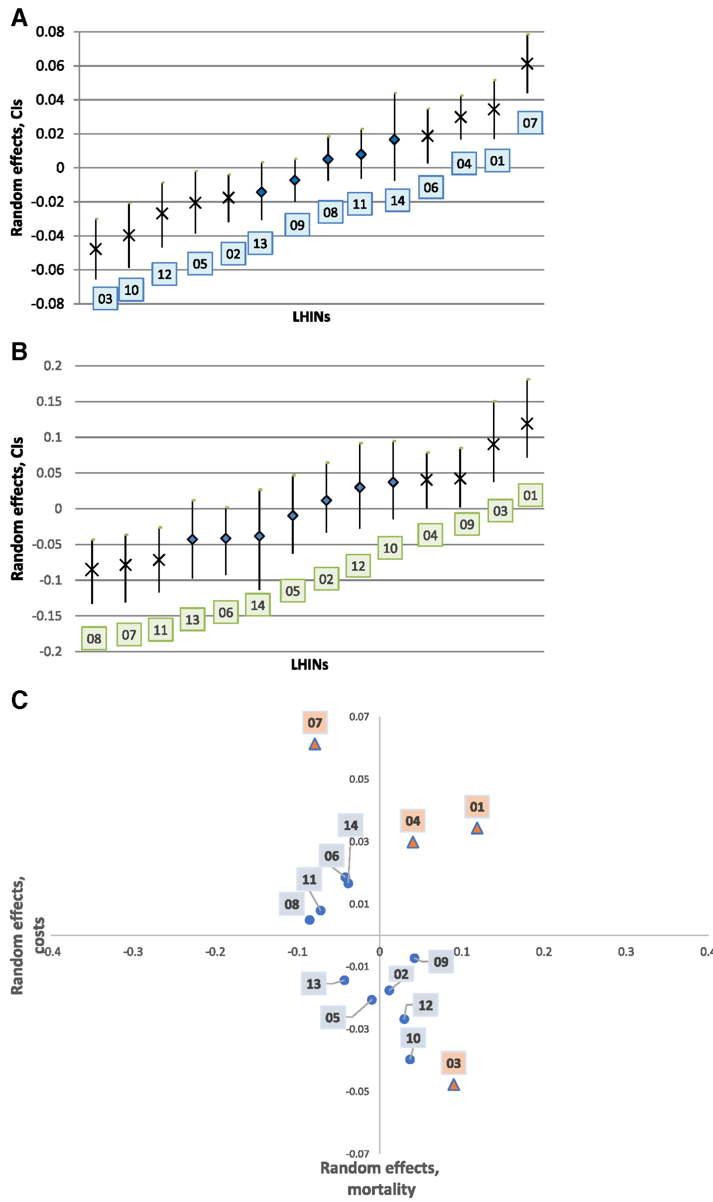


Fig. 2 (See legend on next page.)

(See figure on previous page.)
Fig. 2 a: Ranking LHIN-specific random effects in total costs, HCU. Marked as X are statistically significant. **b**: Ranking LHIN-specific random effects in mortality, HCU. Marked as X are statistically significant. **c**: Cost-mortality relationship, HCU. Both total costs and mortality are adjusted for the regional factor, age, sex, ADGs, and low-income status; colored triangle indicates health district in which variation in both costs and mortality is statistically significant; 01- Erie St. Clair; 02- South West; 03- Waterloo Wellington; 04- Hamilton Niagara Haldimand Brant; 05- Central West; 06-Mississauga Halton; 07- Toronto Central; 08- Central; 09- Central East; 10- South East; 11- Champlain; 12- North Simcoe Muskoka; 13- North East; 14- North West

total costs and mortality (marked as a triangle). Among those LHINs, none were in the lower bottom quadrant ("higher efficiency" pocket). Erie St. Claire 01 and Hamilton 04 LHINs (right upper) spend more and have a higher risk-adjusted mortality. Toronto Central 07 LHIN (left upper) has one of the lowest mortality rates, but it comes at a higher cost compared to other LHINs. In contrast, LHIN 3 had the lowest costs, but one of the highest mortality rates. For non-HCU (Fig. 3a–c), the list of LHINs with significant random effects for both total costs and mortality is broader and different from HCU. Several LHINs in close proximity to the Toronto area exhibit higher efficiency. On the opposite side, South West 02, South East 10, and North East 13 show signs of lower efficiency.

Discussion

This is the first Canadian study to examine geographic variation in healthcare costs and mortality among senior HCU. We found approximately a 14% difference between the highest (100.2 per 1000 seniors) and lowest (88.1 per 1000 seniors) incident senior HCU rates across the LHINs in Ontario. Overall regional variation in total costs and mortality was low in both cohorts, and lower among HCU compared to non-HCU. Our results indicate that traditional drivers of costs and mortality such as age, sex, comorbidity and income play little role in explaining variation in mortality and costs among HCU. Our analyses of individual cost components revealed greater variability in accessing the healthcare system, but, once the patient enters the system, variation in costs was low. Finally, LHINs vary in their costs per mortality rate, which deserves further analysis to determine whether policies or practices followed in high performing LHINs might be usable in other LHINs.

This study's results are important for several reasons. First, when regional variation is of interest, it is important to account for the regional factor in the model. In the literature on geographic healthcare variation, the authors seem to employ fixed effects models more often to describe variation in observed and predicted values through descriptive statistics (coefficient of variation, extremal quotient or its variations, etc.) [15, 20]. The use of mixed effects models is less frequent but provides richer information when applied. As such, in addition to controlling for the regional effect, mixed effects models directly measure regional variability by estimating a variance component. In a two-part mixed effects models such as ours, it is also possible to estimate two components of between-LHIN variation: variation in the probability of costs incurred and variation in costs once incurred. Finally, we ran a fixed effects model in parallel (results available upon a request from authors). Comparing the findings with the mixed effects models showed closely matched coefficient estimates but more narrow standard errors which is an expected difference between the fixed effects and models with random effects.

Second, exploration of regional variation across multiple cost categories among seniors has not been reported for Canadian HCU or the general population. Even internationally, this is rarely done likely due to limited availability of such data. This study results indicate that reporting variation in total spending alone hides the contribution of individual cost components. The magnitude of some cost components such as hospitalization (a mean of $13,677 among HCU) absorbs the variation of smaller components (a mean of $181 in lab costs, respectively). It is particularly so among non-HCU where healthcare expenditures are substantially lower compared to HCU. As shown here, examining regional variation as a function of total costs only would present an incomplete picture: e.g., although small regional variation in total costs, there is a much greater variation in dialysis costs among HCU. Also, comparison with non-HCU points to the fact that there is a very small number of non-HCU patients in several cost categories (e.g., mental health, rehabilitation, etc.) suggesting that incurring costs in these categories may convert a patient into an HCU.

Further, our results indicate that after adjustment, allocation of resources to seniors was similar across Ontario LHINs, more so for HCU compared to non-HCU, which is reassuring for healthcare planners. However, whether the allocation is truly equitable is unclear. Judging by the sign and CIs of coefficients in part 2 of the models, for example, the low- income status was associated with greater intensity of healthcare services across most of the cost components in both cohorts. Also, access to services may be an issue: patients with higher income status are more

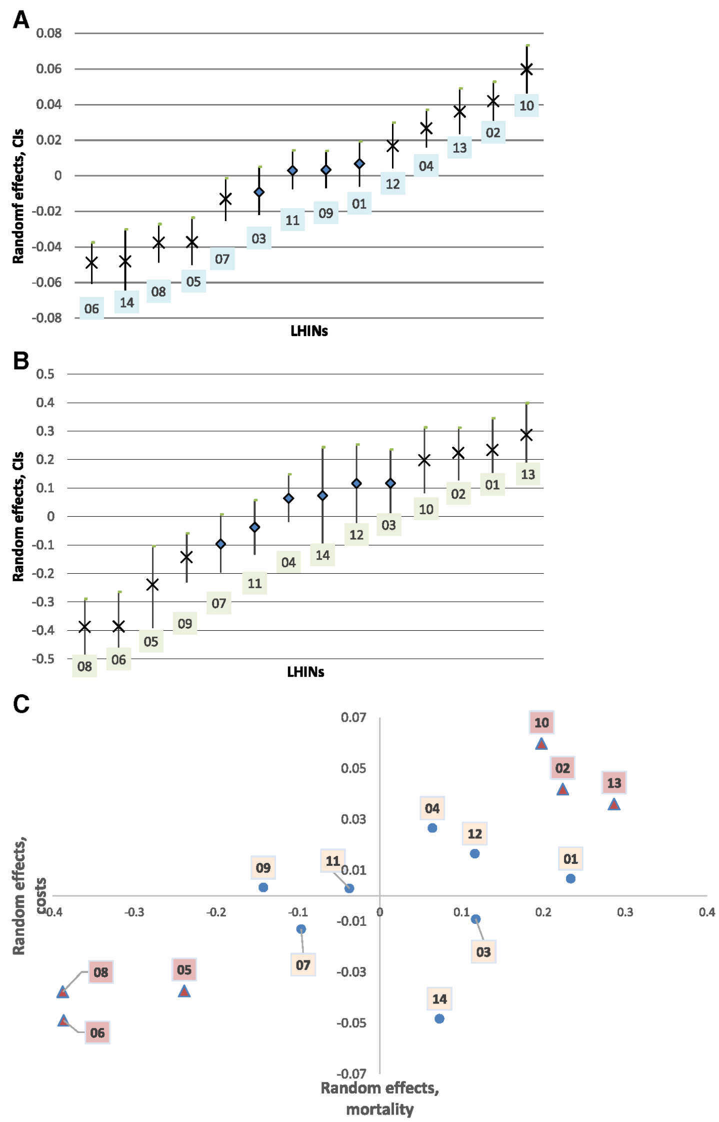


Fig. 3 a: Ranking LHIN-specific random effects in total costs, non-HCU. Marked as X are statistically significant. **b**: Ranking LHIN-specific random effects in mortality, non-HCU. Marked as X are statistically significant. **c**: Cost-mortality relationship, Non-HCU. Both total costs and mortality are adjusted for the regional factor, age, sex, ADGs, and low-income status; colored triangle indicates health district in which variation in both costs and mortality is statistically significant; 01- Erie St. Clair; 02- South West; 03- Waterloo Wellington; 04- Hamilton Niagara Haldimand Brant; 05- Central West; 06- Mississauga Halton; 07- Toronto Central; 08- Central; 09- Central East; 10- South East; 11- Champlain; 12- North Simcoe Muskoka; 13- North East; 14- North West likely to enter the healthcare system. This is aggravated by much higher LHIN-specific variation in the probability of incurring costs. In particular, higher variation in dialysis and cancer costs may be a concern that requires further elucidation.

Finally, we have studied for the first time the relationship between costs and mortality for HCU and non-HCU across Ontario LHINs to explore health system performance from the efficiency angle. Efforts to examine the relationship between healthcare spending and outcomes, most often mortality, have been made globally applying various approaches [16, 30, 59–65]. The approach taken in our study builds on previous research that conducted hospital profiling [57, 58, 66]. As such, our results provide insight into the distribution of mortality in relation to resources spent across the Ontario LHINs by identifying districts of various cost-mortality performance. Although caution should be applied when interpreting the results of the study, e.g., variation in total costs across LHINs appears quite small, the observed differences in efficiency between health regions merit further examination to determine if health improvement could be achieved without additional healthcare spending.

Strengths and limitations

This study has several strengths. First, the dataset contained information on all incident senior HCU in the province at the time of data collection whereas the matched non-HCU represented approximately 25% of the total senior population in the province. Second, the study examines incident HCU cases which represents a shift in the focus of HCU research dominated by studies of persistent cases (those that retain HCU status over time). Since the two populations are likely to be different, studying incident cases of HCU provides important information to inform health policies and interventions. Third, it directly estimates variation across a number of cost categories using two variance components, which has never been done in the past. Finally, to deal with the large proportion of zero costs in the data (i.e. no healthcare use), we used two part-models which have been shown to provide better estimates than models that ignore the over-representation of zeros [48] .

We note some limitations. While the study's cost data captures public expenditures in the most expensive cost categories such as hospital admissions, physician billings, rehabilitation or home care, cost data for some components may be incomplete. For pharmaceutical care, copayment is not included in the ODB cost and, more importantly, the cost of some chemotherapy not covered by the ODB is not captured by the study, especially the costs incurred in outpatient cancer clinics [40]. The LTC costs do not include accommodation charges unless the patient's stay is subsidized by the government. Another Canadian-based study into HCU that used the same source of administrative data but examined the entire HCU population across only 5 cost components estimated the extent of unaccounted for cost data at 7% [7]. However, since data on seniors is usually more complete, our conservative estimate is that less than 5% of government expenditures on individual health services to seniors might not have been included in this study, hence their impact on the results is close to negligible. Secondly, this study did not account for the supply side of the examined variation as the data were not available for analysis. That would require access to LHIN-based data on the number of physicians, hospital and LTC beds, HC/CCAC staff. Instead, our approach standardized for the effect of patient needs. Similarly, we did not have access to several variables which could partially explained some of the variation between LHINs (e.g. patient preferences, health behaviors, education, etc). Further, we encountered model convergence and parameter estimation issues when running models for the non-HCU' cost components using the total non-HCU population. To address this, we re-fitted the models on a random sample of the population. Depending on the cost component, the sample size ranged from 30 to 100%.However, convergence issues in mixed effects models run on the entire population are not uncommon with very large datasets [67]. This is a limitation that in our opinion was alleviated by low discrepancy in the estimates generated by RE models compared to FE models run on the full size of the non-HCU population. Not surprisingly, as 30% of the non-HCU population is still a large enough sample (i.e., > 150,000 individuals). Finally, some may argue that a smaller unit of analysis would be preferable to evaluate regional variation. Using a smaller unit (sub-LHINs in our case) could unmask heterogeneity at the more local level. We did not have information on sub-LHINs and therefore we could not conduct these analyses. However, the choice of LHINs as the unit of analysis is supported by the fact that the boundaries of LHINs were developed with local patterns of care provision in mind [68].

Conclusions

Risk-adjusted allocation of healthcare resources to seniors across Ontario is similar across health districts, more so for HCU than non-HCU. However, when analyzed in combination with risk-adjusted mortality, we identified important variation in the cost-mortality relationship among LHINs which needs to be further explored. The traditional drivers of costs and mortality had a weak impact on the observed variation in the outcomes among both HCU and non-HCU, but largely explained the probability of healthcare system access.

Additional files

Additional file 1: Intra-class coefficients (ICC). Provides details on ICC calculation for costs and mortality. (DOCX 21 kb)

Additional file 2: Model specification and other statistical formulas used in statistical analysis. Provides details on model specification and formulas used in calculations. (DOCX 17 kb)

Additional file 3: A-B. Variation (by LHIN) in patient baseline individual and care characteristics, pre-incident year. The files provide information on the variation in individual and care characteristics between the 14 LHINs: for HCU (2A) and non-HCU (2B). (DOCX 30 kb)

Additional file 4: A-C. Observed and adjusted healthcare care expenditures (total and by cost component) and mortality among HCU and non-HCU, incident year. The file provides details observed and adjusted values and model fit. (DOCX 99 kb)

Additional file 5: Estimate coefficients, healthcare care expenditures among HCU and non-HCU, total costs and cost components, incident year. The file provides details on regression coefficients, including the estimates of variance components. (DOCX 49 kb)

Abbreviations
ACGs: Johns Hopkins Adjusted Clinical Groups; ADGs: Johns Hopkins Aggregated Diagnosis Groups; BC: British Columbia, Canada; CAD: Canadian dollar; CHF: Congestive heart failure; COPD: Chronic obstructive pulmonary disease; CV: Coefficient of variation; DM: Diabetes; EDCs: John Hopkins Expanded Diagnosis Clusters; FY: Fiscal year; GLM: Generalized linear models; HCU: High-cost user; ICC: Intraclass coefficient; ICES: Institute for Clinical Evaluative Sciences; LHIN: Local Health Integration Networks; LRT: Likelihood ratio test; MI: Myocardial infarction; QGIS: Quantum geographic information system; RA: Rheumatoid arthritis; RIO: Rural Index of Ontario; SD: Standard deviation; SDD: Absolute Standardized difference; US: United States

Acknowledgements
Parts of this material are based on data and/or information compiled and provided by the Canadian Institute for Health Information (CIHI). However, the analyses, conclusions, opinions and statements expressed in the material are those of the authors and not necessarily those of CIHI. We thank IMS Brogan Inc. for use of their Drug Information Database.

Funding
This work is supported by personnel funding and in-kind analyst and epidemiologist support from the Ontario Drug Policy Research Network (ODPRN), and personnel awards from the Canadian Institutes of Health Research (CIHR) Drug Safety and Effectiveness Cross-Disciplinary Training (DSECT) Program, the Program for Assessment of Technology in Health (PATH), The Research Institute of St Joe's Hamilton, St Joseph's Healthcare Hamilton, and an Ontario Graduate Scholarship (OGS). The work also is supported by the Institute for Clinical Evaluative Sciences (ICES). ODPRN and ICES are funded by grants from the Ontario Ministry of Health and Long-Term Care (MOHLTC) and the Ontario Strategy for Patient-Orientated Research (SPOR) Support Unit, which is supported by the Canadian Institutes of Health Research and the Province of Ontario. The opinions, results, and conclusions reported in this article are those of the authors and are independent from the funding sources. The funding bodies had no role in the design of the study, the collection, analysis, interpretation of data and in writing the manuscript. No endorsement by the Ontario MOHLTC is intended or should be inferred.

Availability of data and materials
The dataset from this study is held securely in coded form at the Institute for Clinical Evaluative Sciences (ICES). While data sharing agreements prohibit ICES from making the dataset publicly available, access may be granted to those who meet pre-specified criteria for confidential access, available at <http://www.ices.on.ca/DAS>. The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the programs may rely upon coding templates or macros that are unique to ICES.

Authors' contributions
SM, JET, AH, JL, JMP, TG, AC, LM, JRG conceptualized the study. SM, JET, AH, JL, AC, JRG, LM, JMP, TG, WK have contributed to its design. JMP, WK, TG were instrumental in creating datasets. SM prepared the initial draft of the manuscript and revised it based on co- authors' feedback: JET, AH, JL, JMP, TG, JRG, LM, AC, WK provided comments to the initial draft, further revisions, read and approved the final manuscript. The responsibility of study implementation lies with the principal investigator (SM) that is supported and supervised primarily by JET.

Ethics approval and consent to participate
The protocol for this study was reviewed and approved by the Hamilton Integrated Research Ethics Board (ID#1715-C).

Consent for publication
N/A

Competing interests
The authors declare that they have no competing interests.

Publisher's Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details
[1]Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada. [2]Programs for Assessment of Technology in Health (PATH), The Research Institute of St. Joe's Hamilton, St. Joseph's Healthcare, Hamilton, ON, Canada. [3]Division of Geriatric Medicine, Department of Medicine, McMaster University, Hamilton, ON, Canada. [4]Division of Clinical Pharmacology and Toxicology, Department of Medicine, McMaster University, Hamilton, ON, Canada. [5]Geriatric Education and Research in Aging Sciences Centre, Hamilton Health Sciences, Hamilton, ON, Canada. [6]Institute for Clinical Evaluative Sciences (ICES), Toronto, ON, Canada. [7]Center for Health Economics and Policy Analysis (CHEPA), McMaster University, Hamilton, Canada. [8]Département de Médecine Sociale et Préventive, Faculté de Médecine, Université Laval, Quebec City, QC, Canada. [9]Centre de recherche du CHU de Québec, Université Laval, Axe Santé des Populations et Pratiques Optimales en Santé, Québec City, QC, Canada. [10]Biostatistics Unit, Father Sean O'Sullivan Research Centre, St Joseph's Healthcare, Hamilton, ON, Canada. [11]Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada. [12]Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, Canada. [13]Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, ON, Canada.

Received: 2 April 2018 Accepted: 17 October 2018
Published online: 01 November 2018

References
1. Blumenthal D, Chernof B, Fulmer T, Lumpkin J, Selberg J. Caring for high-need, high-cost patients - an urgent priority. N Engl J Med. 2016;375(10):909–11.
2. Hayes SL, Salzberg CA, McCarthy D, et al. High-Need, High-Cost Patients: Who Are They and How Do They Use Health Care? A Population-Based Comparison of Demographics, Health Care Use, and Expenditures. Issue brief (Commonwealth Fund). 2016;26:1–14.
3. Rais S, Nazerian A, Ardal S, Chechulin Y, Bains N, Malikov K. High-cost users of Ontario's healthcare services. Healthcare policy = Politiques de sante. 2013;9(1):44–51.
4. Lee JY, Muratov S, Tarride J-E, Holbrook AM. Managing high-cost healthcare users: the international search for effective evidence-supported strategies. J Am Geriatr Soc. 2018;66(5):1002–8.
5. Statistics Canada: Population by year, by province and territory [http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/demo02a-eng.htm]. Accessed 25 Jan 2018.
6. Roos NP, Shapiro E, Tate R. Does a small minority of elderly account for a majority of health care expenditures? A sixteen-year perspective. The Milbank Quarterly. 1989;67(3–4):347–69.
7. Wodchis WP, Austin PC, Henry DA. A 3-year study of high-cost users of health care. Cmaj. 2016;188(3):182–8.
8. Geographic Variations in Health Care. Focus on Health- OECD Health Policy Studies [https://www.oecd.org/els/health-systems/FOCUS-on-Geographic-Variations-in-Health-Care.pdf]. Accessed 12 Feb 2018.

9. Kim AM, Park JH, Kang S, Hwang K, Lee T, Kim Y. The effect of geographic units of analysis on measuring geographic variation in medical services utilization. J Prev Med Public Health. 2016;49(4):230–9.
10. Lougheed MD, Garvey N, Chapman KR, Cicutto L, Dales R, Day AG, Hopman WM, Lam M, Sears MR, Szpiro K, et al. The Ontario asthma regional variation study: emergency department visit rates and the relation to hospitalization rates. Chest. 2006;129(4):909–17.
11. Feasby TE, Quan H, Ghali WA. Geographic variation in the rate of carotid endarterectomy in Canada. Stroke. 2001;32(10):2417–22.
12. Feinberg AE, Porter J, Saskin R, Rangrej J, Urbach DR. Regional variation in the use of surgery in Ontario. CMAJ open. 2015;3(3):E310–6.
13. Hogan DB, Maxwell CJ, Fung TS, Ebly EM. Regional variation in the use of medications by older Canadians--a persistent and incompletely understood phenomena. Pharmacoepidemiol Drug Saf. 2003;12(7):575–82.
14. Morgan SG, Cunningham CM, Hanley GE. Individual and contextual determinants of regional variation in prescription drug use: an analysis of administrative data from British Columbia. PLoS One. 2010; 5(12):e15883.
15. Newhouse JP, Garber AM, Graham RP, McCoy MA, Mancher M, Kibria A. Variation in health care spending: target decision making, not geography. In: Committee on geographic variation in health care spending and promotion of high-value care; board on health care services; institute of Medicine; 2013.
16. Elliott S, Fisher M, David E, Wennberg M, Thrse A, Stukel P, Daniel J, Gottlieb MFL, Lucas P, Étoile L, Pinder M. The implications of regional variations in Medicare spending. Part 2: health outcomes and satisfaction with care. Ann Intern Med. 2003;138(4):288–98.
17. Fisher E, Goodman D, Skinner J, Bronner K. Health Care Spending, Quality, and Outcomes. The Dartmouth Insititute for Health Policy Research and Clinical Practice, 2009.
18. Fisher ES, Wennberg DE, Stukel TA, Gottlieb DJ, Lucas FL, Pinder ÉL. The implications of regional variations in Medicare spending. Part 1: the content, quality, and accessibility of care. Ann Intern Med. 2003;138(4):273–87.
19. Zuckerman SWT, Berenson R, Hadle J. Clarifying sources of geographic differences in Medicare spending. N Engl J Med. 2010;363:54–62.
20. Lavergne MR, Barer M, Law MR, Wong ST, Peterson S, McGrail K. Examining regional variation in health care spending in British Columbia, Canada. Health Policy. 2016;120(7):739–48.
21. Brooks GA, Li L, Uno H, Hassett MJ, Landon BE, Schrag D. Acute hospital care is the chief driver of regional spending variation in Medicare patients with advanced cancer. Health affairs (Project Hope). 2014;33(10):1793–800.
22. Ellis RP, Fiebig DG, Johar M, Jones G, Savage E. Explaining health care expenditure variation: large-sample evidence using linked survey and health administrative data. Health Econ. 2013;22(9):1093–110.
23. Bevan G: Using information on variation in rates of supply to questoin professional discretion in public services. 2004.
24. Kephart G, Asada Y. Need-based resource allocation: different need indicators, different results? BMC Health Serv Res. 2009;9:122.
25. O'Neill J, Tabish H, Welch V, Petticrew M, Pottie K, Clarke M, Evans T, Pardo Pardo J, Waters E, White H, et al. Applying an equity lens to interventions: using PROGRESS ensures consideration of socially stratifying factors to illuminate inequities in health. J Clin Epidemiol. 2014;67(1):56–64.
26. Struikmans H, Aarts MJ, Jobsen JJ, Koning CC, Merkus JW, Lybeert ML, Immerzeel J, Poortmans PM, Veerbeek L, Louwman MW, et al. An increased utilisation rate and better compliance to guidelines for primary radiotherapy for breast cancer from 1997 till 2008: a population-based study in the Netherlands. Radiother Oncol. 2011;100(2):320–5.
27. Bierman AS, Shack AR, Johns A, for the POWER Study. Achieving health equity in Ontario: opportunities for intervention and improvement. In: Bierman AS, editor. Project for an Ontario Women's health evidence-based report. Volume 2 ed. Toronto: St. Michael's Hospital and the Institute for Clinical Evaluative Sciences; 2012.
28. Ohinmaa A, Zheng Y, Jeerakathil T, Klarenbach S, Hakkinen U, Nguyen T, Friesen D, Ruseski J, Kaul P, Ariste R, et al. Trends and regional variation in hospital mortality, length of stay and cost in Hospital of Ischemic Stroke Patients in Alberta accompanying the provincial reorganization of stroke care. J Stroke Cerebrovasc Dis. 2016;25(12):2844–50.
29. Joumard, I., André C., Nicq C. "Health Care Systems: Efficiency and Institutions", OECD Economics Department Working Papers, No. 769. Paris: OECD Publishing; 2010. https://doi.org/10.1787/5kmfp51f5f9t-en.
30. Allin S, Veillard J, Wang L, Grignon M. How can health system efficiency be improved in Canada? Healthcare Policy. 2015;11(1):33–45.
31. Zhang Y, Baik SH, Fendrick AM, Baicker K. Comparing local and regional variation in health care spending. N Engl J Med. 2012;367(18):1724–31.
32. Hong YR, Kates F, Song SJ, Lee N, Duncan RP, Marlow NM. Benchmarking implications: analysis of Medicare accountable care organizations spending level and quality of care. J Healthc Qual. 2018. https://doi.org/10.1097/JHQ.0000000000000123. [Epub ahead of print].
33. Skinner J. Causes and consequences of regional variations in health care. In: Handbook of health economics, vol. 2011. Volume 2 ed. p. 45–93.
34. Corallo AN, Croxford R, Goodman DC, Bryan EL, Srivastava D, Stukel TA. A systematic review of medical practice variation in OECD countries. Health Policy. 114(1):5–14.
35. Rosenberg BL, Kellar JA, Labno A, Matheson DH, Ringel M, VonAchen P, Lesser RI, Li Y, Dimick JB, Gawande AA, et al. Quantifying geographic variation in health care outcomes in the United States before and after risk-adjustment. PLoS One. 2016;11(12):e0166762.
36. Muratov S, Lee J, Holbrook A, Paterson JM, Guertin JR, Mbuagbaw L, Gomes T, Khuu W, Pequeno P, Costa AP, et al. Senior high-cost healthcare users' resource utilization and outcomes: a protocol of a retrospective matched cohort study in Canada. BMJ Open. 2017;7(12):e018488.
37. Fitzpatrick T, Rosella LC, Calzavara A, Petch J, Pinto AD, Manson H, Goel V, Wodchis WP. Looking beyond income and education: socioeconomic status gradients among future high-cost users of health care. Am J Prev Med. 2015;49(2):161–71.
38. Rosella LC, Fitzpatrick T, Wodchis WP, Calzavara A, Manson H, Goel V. High-cost health care users in Ontario, Canada: demographic, socio-economic, and health status characteristics. BMC Health Serv Res. 2014;14:532.
39. Institute for Clinical Evaluative Sciences (ICES); www.ices.on.ca . Accessed 10 Dec 2017.
40. Wodchis WP, Bushmeneva K, Nikitovic M, McKillop I. Guidelines on person-level costing using administrative databases in Ontario. In: Working Paper Series, vol. 1. Toronto: Health System Performance Research Network; 2013.
41. Ontario's Local Health Integration Networks. [www.lhins.on.ca]. Accessed 6 Feb 2018.
42. Local Health System Integration Act, 2006, S.O. 2006, c. 4 (amended 2017). [https://www.ontario.ca/laws/statute/06l04]. Accessed 26 Jan 2018.
43. Kralj B. Measuring 'rurality' for purposes of health-care planning: an empirical measure for Ontario. Ont Med Rev. 2000;67(9):33–52.
44. The Johns Hopkins ACG® System Version 10.0 Technical Reference Guide. In.: Department of Health Policy and Management, Johns Hopkins University, Bloomberg School of Public Health; 2014.
45. Gershon AS, Wang C, Guan J, Vasilevska-Ristovska J, Cicutto L, TO T. Identifying individuals with physcian diagnosed COPD in health administrative databases. Copd. 2009;6(5):388–94.
46. Schultz SE, Rothwell DM, Chen Z, Tu K. Identifying cases of congestive heart failure from administrative data: a validation study using primary care patient records. Chronic Dis Inj Can. 2013;33(3):160–6.
47. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med. 2009;28(25):3083–107.
48. Buntin MB, Zaslavsky AM. Too much ado about two-part models and transformation? Comparing methods of modeling Medicare expenditures. J Health Econ. 2004;23(3):525–42.
49. Liu L, Cowen ME, Strawderman RL, Shih Y-CT. A flexible two-part random effects model for correlated medical costs. J Health Econ. 2010;29(1):110–23.
50. Basu A, Manning WG, Mullahy J. Comparing alternative models: log vs cox proportional hazard? Health Econ. 2004;13(8):749–65.
51. Gregori D, Petrinco M, Bo S, Desideri A, Merletti F, Pagano E. Regression models for analyzing costs and their determinants in health care: an introductory review. Int J Qual Health Care. 2011;23(3):331–41.
52. de Vries EF, Heijink R, Struijs JN, Baan CA. Unraveling the drivers of regional variation in healthcare spending by analyzing prevalent chronic diseases. BMC Health Serv Res. 2018;18(1):323.
53. Liu L, Ma JZ, Johnson BA. A multi-level two-part random effects model, with application to an alcohol-dependence study. Stat Med. 2008;27(18): 3528–39.
54. Tooze JA, Grunwald GK, Jones RH. Analysis of repeated measures data with clumping at zero. Stat Methods Med Res. 2002;11(4):341–55.
55. Austin PC, Merlo J. Intermediate and advanced topics in multilevel logistic regression analysis. Stat Med. 2017;36(20):3257–77.
56. Nakagawa S, Johnson PCD, Schielzeth H. The coefficient of determination R2 and intra-class correlation coefficient from generalized linear mixed-effects models revisited and expanded. J R Soc Interface. 2017;14(134): 20170213.

57. D'Errigo P, Tosti ME, Fusco D, Perucci CA, Seccareccia F. Use of hierarchical models to evaluate performance of cardiac surgery centres in the Italian CABG outcome study. BMC Med Res Methodol. 2007;7:29.
58. MacKenzie TA, Grunkemeier GL, Grunwald GK, O'Malley AJ, Bohn C, Wu Y, Malenka DJ. A primer on using shrinkage to compare in-hospital mortality between centers. Ann Thorac Surg. 2015;99(3):757–61.
59. Hadley J, Reschovsky JD. Medicare spending, mortality rates, and quality of care. Int J Health Care Finance Econ. 2012;12(1):87–105.
60. Lippi G, Mattiuzzi C, Cervellin G. No correlation between health care expenditure and mortality in the European Union. Eur J Intern Med. 2016;32:e13–4.
61. Gallet CA, Doucouliagos H. The impact of healthcare spending on health outcomes: a meta-regression analysis. Soc Sci Med. 2017;179:9–17.
62. Cohen D, Manuel DG, Tugwell P, Sanmartin C, Ramsay T. Does higher spending improve survival outcomes for myocardial infarction? Examining the cost-outcomes relationship using time-varying covariates. Health Serv Res. 2015;50(5):1589–605.
63. Stargardt T, Schreyogg J, Kondofersky I. Measuring the relationship between costs and outcomes: the example of acute myocardial infarction in German hospitals. Health Econ. 2014;23(6):653–69.
64. Stukel TA, Fisher ES, Alter DA, Guttmann A, Ko DT, Fung K, Wodchis WP, Baxter NN, Earle CC, Lee DS. Association of Hospital Spending Intensity with Mortality and Readmission Rates in Ontario hospitals. Jama. 2012;307(10):1037–45.
65. McKay NL, Deily ME. Comparing high- and low-performing hospitals using risk-adjusted excess mortality and cost inefficiency. Health Care Manag Rev. 2005;30(4):347–60.
66. Zhang M, Strawderman RL, Cowen ME, Wells MT. Bayesian inference for a two-part hierarchical model. J Am Stat Assoc. 2006;101(475):934–45.
67. Gebregziabher M, Egede L, Gilbert GE, Hunt K, Nietert PJ, Mauldin P. Fitting parametric random effects models in very large data sets with application to VHA national data. BMC Med Res Methodol. 2012;12:163.
68. Health Analyst's Toolkit. In.: Health Analytics Branch, Ontario Ministry of Health and Long-Term Care; 2012.

Appendix 1: Intra-class coefficients (ICC)

A. Costs

	Parameters	Total	Hosp	MD	HC	ODB	ED	Lab	LTC	MH	Rehab	Dialysis	Cancer	CCC
HCU	**Random intercept, subject=LHIN**	0.0012	0.0013	0.0170	0.0073	0.0015	0.0018	0.0110	0.0010	0.01966	0.0084	0.3000	0.0236	0.0358
	Residual	0.4596	0.7708	0.3929	0.9227	1.1425	0.4521	0.6176	0.7640	0.7687	0.013	0.126	0.021	0.037
	ICC, %	0.26%	0.17%	4.15%	0.79%	0.13%	0.40%	1.74%	0.13%	2.49%	1.26%	12.61%	2.05%	3.70%
	p-value (random intercept)	0.001	0.027	0.007	0.008	0.026	0.02	0.006	0.36	0.98	0.656	2.080	1.124	0.93
Non-HCU	**Random intercept, subject=LHIN**	0.0010	0.0029	0.0140	0.0140	0.0017	0.0018	0.0087	not defined	not defined	0.0003	0.4641	0.2264	not defined
	p-value (random intercept)	0.012	0.024	0.005	0.008	0.001	0.02	0.005			0.47	0.09	0.019	
	Residual	0.7110	0.5554	0.5448	0.5860	1.2780	0.4521	0.5288			0.0029	0.2694	0.8596	
	ICC, %	0.14%	0.53%	2.51%	2.33%	0.13%	0.40%	1.61%			8.29%	63.27%	20.85%	

ICC=estimate of random intercept/residual+ estimate of random intercept (%)

Abbreviations: Hosp- hospitalization costs, MD-physician costs, HC-home care, ODB-Outpatient Drug Benefit, ED- emergency department, LTC-long-term care, MH-mental health, CCC-complex continuing care

B. Mortality

Parameters	HCU	Non-HCU
Random intercept, subject=LHIN	0.004159	0.04208
p-value (random intercept)	0.017	0.009
Residual	3.29	3.29
ICC, %	0.126%	1.263%

Appendix 2: Model specification and other statistical formulas used in statistical analysis

A. General equation

$$y_{ij}=(\beta 0+u0_j) + \sum\beta_{ij}X_{ij}+e_{ij}$$

where y_{ij} –is the outcome (costs or mortality) in patient i from LHIN_j; $\beta 0$ – the provincial mean; $u0_j$ – is the random effect for each LHIN that is assumed $u0j \sim N(0, \sigma^2{}_u)$; β_{ij} - are the fixed effects of individual level characteristics; X_{ij} - is the vector of covariates at the individual level; e_{ij} - is the residual error.

B. Coefficient of determination (R2)

a. Binary outcome (e.g., mortality)

$$R2 = \frac{\sigma 2fe}{\sigma 2u + \sigma 2fe + \pi 2/3}$$

b. Continuous outcome with gamma distribution (i.e., costs)

$$R2 = \frac{\sigma 2fe}{\sigma 2u + \sigma 2fe + \ln(1 + \frac{1}{v})}$$

where $\sigma 2fe$- variance explained by fixed effects; $\sigma 2u$- variance explained by random effects (LHINs); v- the shape parameter from gamma GLM

Additional files 3A-B. **Variation (by LHIN) in patient baseline individual and care characteristics, pre-incident year**

A: HCU

	LHIN	Age (%)			Sex (F, %)	Rurality (% of urban)	Low income senior (%)	Number of ADGs, mean per patient	Proportion with chronic conditions (%)			Number of physicians involved in care, mean per patient	Seen by a geriatrician (%)	Number of prescription drugs, mean per patient	Acute inpatient admissions (%)
		66-74	75-84	≥85					Malignant neoplasms	Common chronic conditions*	Mental health#				
1	Erie St. Clair	39.9	39.4	20.8	53.6	32.7	13.6	10.6	33.1	65.3	40.1	8.3	0.5	9.0	3.5
2	South West	38.8	39.7	21.6	53.5	39.5	14.7	9.9	37.3	59.2	35.6	7.5	2.6	8.0	4.1
3	Waterloo Wellington	37.9	40.4	21.7	53.4	75.9	14.3	9.6	33.0	58.3	34.2	7.3	4.1	7.9	3.4
4	Hamilton Niagara	38.1	40.1	21.7	53.8	76.8	14.1	10.2	32.7	60.1	36.9	8.1	3.5	8.4	3.5
5	Central West	44.5	38.9	16.6	51.3	91.1	28.1	10.4	26.8	63.2	40.6	8.3	3.3	9.2	3.5
6	Mississauga Halton	38.4	39.8	21.8	52.6	100.0	19.5	10.5	31.1	59.0	40.4	8.5	5.0	8.6	3.6
7	Toronto Central	36.5	39.2	24.3	55.4	100.0	25.7	10.4	32.8	57.0	45.1	8.5	3.6	8.3	2.8
8	Central	36.3	40.6	23.1	53.1	87.4	23.9	10.8	31.8	59.6	42.4	8.9	3.9	8.8	2.9
9	Central East	38.0	40.8	21.3	52.4	60.1	21.2	10.3	31.8	62.6	37.3	8.6	2.6	8.8	2.8
10	South East	42.4	39.6	18.0	50.7	33.8	14.8	9.6	31.5	60.1	33.6	8.1	1.2	8.1	2.7
11	Champlain	39.3	38.3	22.4	53.5	64.4	14.9	10.1	33.4	58.4	39.6	8.4	1.3	8.1	3.3
12	North Simcoe Muskoka	43.0	39.8	17.3	52.1	22.6	13.7	9.9	34.9	60.6	35.5	7.4	2.2	7.9	4.5
13	North East	42.6	41.3	16.1	51.2	25.1	16.3	9.8	28.5	63.9	35.9	7.2	1.5	8.5	6.0
14	North West	39.8	40.3	19.9	51.1	56.3	11.1	9.9	29.9	61.6	28.9	7.9	4.3	7.9	6.4
CV		**6.3%**	**2%**	**12.3%**	**2.5%**	**44.7%**	**29.7%**	**3.7%**	**8.1%**	**4.0%**	**11.0%**	**6.5%**	**47.8%**	**5.2%**	**30.0%**

ADGs- Aggregated Diagnosis Groups; CV- Coefficient of Variation; HCU- high-cost user; *ICES- derived common chronic conditions (CHF- congestive heart failure; COPD- chronic obstructive pulmonary disease; DM- diabetes, MI- myocardial infarction, RA- rheumatoid arthritis); LHIN – Local Health Integrated Network; SD- Standard Deviation; # includes any of mental health conditions among Expanded Diagnosis Clusters (PSY01-12)

B: Non-HCU

	LHIN	Age (%)			Sex (F, %)	Rurality (% of urban)	Low income senior (%)	Comorbidity (# of ADGs), mean per patient	Proportion with chronic conditions (%)			Number of MDs involved in care, mean per patient	Seen by a geriatrician (%)	Number of prescription drugs, mean per patient	Acute inpatient admissions (%)
		66-74	75-84	≥85					Malignant neoplasms	Common chronic conditions*	Mental health#				
1	Erie St. Clair	39.9	39.4	20.8	53.6	34.6	13.1	8.4	25.6	49.2	31.2	6.0	0.3	6.2	2.1
2	South West	38.8	39.7	21.6	53.5	40.2	12.9	8.1	29.3	44.9	26.4	5.4	1.1	5.6	2.3
3	Waterloo Wellington	37.9	40.4	21.7	53.4	76.8	13.4	7.6	24.7	42.3	24.4	5.2	1.9	5.3	1.9
4	Hamilton Niagara	38.1	40.1	21.7	53.8	75.9	13.2	8.3	25.8	44.1	27.9	6.0	1.4	5.8	2.0
5	Central West	44.5	38.9	16.6	51.3	93.3	27.5	7.7	17.3	46.1	27.0	5.5	1.1	5.9	1.7
6	Mississauga Halton	38.4	39.8	21.8	52.6	100.0	18.4	7.7	20.4	42.5	27.1	5.5	1.9	5.3	1.7
7	Toronto Central	36.5	39.2	24.3	55.4	100.0	25.2	7.5	21.5	42.1	29.9	5.4	1.3	5.2	1.4
8	Central	36.3	40.6	23.1	53.1	90.0	24.6	7.9	20.5	43.4	28.3	5.8	1.4	5.6	1.5
9	Central East	38.0	40.8	21.3	52.4	67.1	22.2	7.9	22.6	46.8	26.6	5.8	1.1	5.9	1.4
10	South East	42.4	39.6	18.0	50.7	33.2	12.6	7.9	24.1	44.2	25.0	6.0	0.6	5.5	1.8
11	Champlain	39.3	38.3	22.4	53.5	69.1	14.3	7.9	24.1	42.4	28.3	5.8	0.5	5.3	1.6
12	North Simcoe Muskoka	43.0	39.8	17.3	52.1	21.7	11.9	8.1	28.2	45.5	27.3	5.5	1.0	5.5	2.5
13	North East	42.6	41.3	16.1	51.2	26.2	15.6	7.9	21.9	48.4	25.9	5.3	0.5	5.9	3.4
14	North West	39.8	40.3	19.9	51.1	50.4	10.8	7.6	21.5	46.0	20.7	5.5	1.9	5.1	3.4
CV		**6.3%**	**2.0%**	**12.3%**	**2.5%**	**44.7%**	**33.6%**	**3.5%**	**13.8%**	**5.1%**	**9.3%**	**4.6%**	**48.4%**	**5.7%**	**31.8%**

ADGs- Aggregated Diagnosis Groups; CV- Coefficient of Variation; HCU- high-cost user; *ICES- derived common chronic conditions (CHF- congestive heart failure; COPD- chronic obstructive pulmonary disease; DM- diabetes, MI- myocardial infarction, RA- rheumatoid arthritis); LHIN – Local Health Integrated Network; SD- Standard Deviation; # includes any of mental health conditions among Expanded Diagnosis Clusters (PSY01-12)

Additional files 4A-B **Observed and adjusted healthcare care expenditures (total and by cost component) and mortality among HCUs and non-HCUs, incident year**

A: HCU

Models are adjusted for random effects (RE), age, sex, ADGs, and low-income status; AIC/BIC- Akaike/Bayesian information criterion; CV- Coefficient of variation; HCU- high-cost user, LL- loglikelihood; ODB-Outpatient Drug Benefit plan; SD- standard deviation;

LHIN		Total costs			Hospital admission			Physician			Home care		
		Obs	RE	Adj	Obs	RE	Adj	Obs	RE	Adj	Obs	RE	Adj
	Proportion of zero values (%)	0.0			11.7			0.03			41.6		
1	Erie St. Clair	30,559	30,518	30,510	14,204	14,165	14,175	4,152	4,151	4,138	1,771	1,772	1,780
2	South West	29,136	29,151	29,204	13,620	13,634	13,654	3,575	3,576	3,566	1,991	1,989	1,988
3	Waterloo Wellington	28,305	28,373	28,459	12,798	12,864	12,925	3,852	3,853	3,844	1,800	1,800	1,798
4	Hamilton Niagara	30,576	30,557	30,546	13,539	13,534	13,553	4,171	4,171	4,169	2,156	2,153	2,129
5	Central West	28,773	28,820	28,813	13,441	13,469	13,439	4,875	4,872	4,883	1,570	1,574	1,565
6	Mississauga Halton	30,251	30,227	30,175	13,291	13,319	13,305	4,655	4,654	4,675	1,460	1,464	1,479
7	Toronto Central	31,813	31,737	31,649	13,536	13,511	13,411	4,703	4,702	4,720	1,916	1,912	1,917
8	Central	29,785	29,781	29,771	13,164	13,174	13,146	4,851	4,850	4,867	1,618	1,619	1,618
9	Central East	29,487	29,490	29,481	13,286	13,298	13,290	4,371	4,371	4,371	1,551	1,553	1,556
10	South East	28,434	28,495	28,523	13,003	13,022	13,043	3,861	3,861	3,852	2,001	1,996	1,981
11	Champlain	29,929	29,921	29,926	13,652	13,632	13,638	4,047	4,047	4,048	1,579	1,581	1,587
12	North Simcoe Muskoka	28,647	28,708	28,752	13,774	13,796	13,820	4,124	4,124	4,118	1,742	1,742	1,731
13	North East	29,109	29,133	29,165	14,833	14,795	14,834	3,344	3,346	3,343	1,663	1,665	1,664
14	North West	30,238	30,165	30,187	15,338	15,130	15,171	3,171	3,176	3,188	1,810	1,808	1,815
	Mean	29,646	29,648	29,654	13,677	13,667	13,672	4,125	4,125	4,127	1,759	1,759	1,758
	SD	992.8	948.9	913.6	694.6	639.7	651.7	536.4	534.8	541.0	201.8	199.3	193.2
	CV	3.3	3.2	3.1	5.1	4.7	4.8	13.0	13.0	13.1	11.5	11.3	11.0
	-2 Log Likelihood	3925362	3925073	3922740	3426248	3425853	3422126	3221763	3216335	3209694	2090097	2087329	2067947
	AIC (smaller is better)	3925366	3925079	3922754	3426254	3425865	3422154	3221767	3216341	3209708	2090103	2087341	2067975
	BIC (smaller is better)	3925386	3925080	3922758	3426284	3425869	3422162	3221787	3216343	3209712	2090133	2087344	2067984
	LRT (Chi2 dist, p<0.05)		289.2	2333.0		394.6	3727.4		5428.2	6640.9		2768.4	19381.3

LHIN		ODB			Emergency department			Mental health			Lab		
		Obs	RE	Adj	Obs	RE	Adj	Obs	RE	Adj	Obs	RE	Adj
	Proportion of zero values (%)	0.9			24.3			99.0			14.4		
1	Erie St. Clair	2,553	2,549	2,559	895	894	893	194	207	207	177	177	177
2	South West	2,301	2,306	2,302	865	866	864	324	313	313	149	150	150
3	Waterloo Wellington	2,401	2,406	2,395	823	824	823	345	313	312	199	199	199
4	Hamilton Niagara	2,535	2,533	2,544	840	840	842	207	212	210	198	198	197
5	Central West	2,527	2,524	2,532	823	823	824	151	178	180	209	208	208
6	Mississauga Halton	2,395	2,396	2,394	825	826	825	266	261	257	214	214	214
7	Toronto Central	2,283	2,283	2,270	852	852	855	351	333	332	170	170	171
8	Central	2,422	2,423	2,415	816	816	818	232	235	237	221	220	220
9	Central East	2,505	2,503	2,505	835	835	835	186	195	193	212	212	212
10	South East	2,590	2,582	2,587	863	863	862	269	262	257	164	164	164
11	Champlain	2,566	2,563	2,571	888	887	886	356	341	341	162	162	162
12	North Simcoe Muskoka	2,466	2,464	2,467	859	860	859	286	275	280	184	184	184
13	North East	2,474	2,472	2,478	915	915	912	214	223	229	145	145	146
14	North West	2,103	2,144	2,131	1,099	1,087	1,089	161	204	197	128	129	129
	Mean	2,437	2,439	2,439	871	871	870	253	254	253	181	181	181
	SD	134.5	124.7	132.0	71.9	69.0	69.1	71.5	54.3	54.5	29.0	28.8	28.5
	CV	5.5	5.1	5.4	8.3	7.9	7.9	28.2	21.4	21.5	16.0	15.9	15.7
	-2 Log Likelihood	3088995	3088721	3084420	2295081	2294521	2287076	58709	58656	58378	2049266	2043455	2037745
	AIC (smaller is better)	3089001	3088733	3084448	2295087	2294533	2287104	58715	58668	58406	2049272	2043467	2037773
	BIC (smaller is better)	3089031	3088737	3084457	2295118	2294537	2287113	58745	58672	58415	2049302	2043471	2037781
	LRT (Chi2 dist, p<0.05)		273.7	4300.8		560.6	7445.3		53.0	278.2		5811.1	5710.6

LHIN		Dialysis			Cancer			LTC			CCC			Rehabilitation		
		Obs	RE	Adj	Obs	RE	Adj	Obs	RE	Adj	Obs	RE	Adj	Obs	RE	Adj
	Proportion of zero values (%)	99.3			90.1			93.4			95.4			92.5		
1	Erie St. Clair	158	132	128	1,189	1,190	1,199	1,062	1,064	1,064	1,093	1,085	1,079	1,849	1,832	1,819
2	South West	83	92	91	1,355	1,291	1,319	1,254	1,245	1,248	758	769	771	994	1,003	1,003
3	Waterloo Wellington	99	101	102	1,536	1,516	1,527	1,165	1,135	1,141	1,073	1,079	1,086	950	959	958
4	Hamilton Niagara	133	126	125	1,291	1,276	1,285	1,066	1,061	1,063	1,760	1,756	1,757	1,048	1,040	1,035
5	Central West	146	128	132	1,207	1,222	1,231	844	884	871	527	550	547	1,026	1,052	1,053
6	Mississauga Halton	81	84	85	1,474	1,468	1,462	793	815	819	1,188	1,178	1,175	2,015	1,987	1,971
7	Toronto Central	58	78	78	1,125	1,173	1,131	735	744	756	2,211	2,178	2,171	1,785	1,792	1,804
8	Central	121	115	112	1,181	1,192	1,178	921	921	924	950	950	952	1,581	1,585	1,593
9	Central East	99	101	102	1,206	1,233	1,227	1,101	1,070	1,065	1,010	1,012	1,013	1,821	1,817	1,828
10	South East	125	113	115	1,118	1,184	1,206	1,048	982	963	791	811	810	719	737	732
11	Champlain	56	76	75	1,298	1,271	1,268	987	984	991	725	718	718	1,709	1,702	1,698
12	North Simcoe Muskoka	92	98	99	1,254	1,239	1,281	1,021	1,071	1,066	593	604	604	777	793	794
13	North East	85	94	98	1,140	1,159	1,183	1,063	1,095	1,087	773	769	772	821	809	802
14	North West	197	153	150	1,256	1,235	1,276	724	815	812	1,687	1,664	1,659	858	866	869
	Mean	109	106	107	1,259	1,261	1,269	985	992	991	1,081	1,080	1,080	1,282	1,284	1,283
	SD	39.6	22.2	21.7	125.2	106.3	108.6	160.2	141.0	140.4	488.0	475.5	473.8	476.5	467.4	467.5
	CV	36.2	20.9	20.3	9.9	8.4	8.6	16.3	14.2	14.2	45.1	44.0	43.9	37.2	36.4	36.4
	-2 Log Likelihood	38786	37751	37613	477492	476322	472853	332125	331899	322971	244232	243120	240498	379798	378292	376573
	AIC (smaller is better)	38792	37763	37641		476334	472881		331911	322999	244238	243132	240526	379804	378304	376601
	BIC (smaller is better)	38822	37767	37650		476337	472890		331915	323008	244268	243136	240535	379835	378308	376610
	LRT (Chi2 dist, p<0.05)		1035.2	138.1		1170.7	3468.5		225.9	8928.5		1111.6	2622.1		1506.3	1719.0

B: Non-HCU

	LHIN	Total costs (30% sample)			Hospital admission (50% sample)			Physician (100% sample)			Home care (75% sample)		
		Obs	RE	Adj	Obs	RE	Adj	Obs	RE	Adj	Obs	RE	Adj
	Proportion of zero values (%)	9.4			85.9			10.50			92.5		
1	Erie St. Clair	2,558	2,553	2,601	248	248	249	811	811	818	135	135	135
2	South West	2,593	2,590	2,621	263	262	260	739	739	749	148	148	147
3	Waterloo Wellington	2,408	2,418	2,431	242	242	242	772	772	785	146	145	146
4	Hamilton Niagara	2,633	2,629	2,658	241	240	239	843	843	848	139	139	138
5	Central West	2,348	2,350	2,348	188	188	191	830	830	821	93	94	93
6	Mississauga Halton	2,266	2,273	2,260	192	193	193	807	807	803	82	83	84
7	Toronto Central	2,323	2,319	2,321	142	143	144	798	799	789	130	130	131
8	Central	2,414	2,411	2,414	173	173	176	849	849	839	120	120	120
9	Central East	2,444	2,442	2,458	206	207	208	829	829	827	134	134	134
10	South East	2,565	2,564	2,589	266	267	267	769	769	781	135	134	133
11	Champlain	2,451	2,449	2,458	211	211	212	735	735	740	118	118	119
12	North Simcoe Muskoka	2,561	2,561	2,592	280	279	276	820	819	825	88	89	89
13	North East	2,514	2,515	2,534	332	332	330	631	631	644	121	121	120
14	North West	2,217	2,262	2,273	312	303	302	517	520	528	128	128	127
	Mean	2,450	2,453	2,468	235	235	235	768	768	771	123	123	123
	SD	128.0	120.3	134.0	53.5	52.3	50.9	92.3	91.4	87.6	21.1	20.5	20.3
	CV	5.2	4.9	5.4	22.7	22.3	21.7	12.0	11.9	11.4	17.2	16.7	16.6
	-2 Log Likelihood	2644680	2642366	2553865	834313	832874	821522	1905951	1902381	1832307	708186	706833	674824
	AIC (smaller is better)	2644686	2642378	2553893	834319	832886	821550	1905957	1902393	1832335	708192	706845	674852
	BIC (smaller is better)	2644716	2642381	2553902	834350	832890	821559	1905987	1902397	1832344	708224	706849	674861
	LRT (Chi2 dist, p<0.05)		2314.1	88500.6		1438.6	11352.1		3570.0	70073.9		1352.4	32008.9

LHIN		**ODB (50% sample)**			**Emergency department (40% sample)**			**Mental health**			**Lab (100% sample)**		
		Obs	RE	Adj	Obs	RE	Adj	Obs	RE	Adj	Obs	RE	Adj
	Proportion of zero values (%)	15.6			79.6						31.1		
1	Erie St. Clair	931	927	935	103	103	103				98	98	99
2	South West	864	865	873	118	119	119				88	88	89
3	Waterloo Wellington	830	832	834	94	93	93				105	105	105
4	Hamilton Niagara	901	900	905	101	101	102				114	114	114
5	Central West	844	841	846	68	69	69				107	107	106
6	Mississauga Halton	810	810	807	74	74	74				115	115	114
7	Toronto Central	761	763	759	74	74	74				98	98	98
8	Central	823	823	819	74	74	74				117	117	116
9	Central East	897	895	898	85	85	85				114	114	114
10	South East	859	861	866	111	112	111				93	93	94
11	Champlain	830	830	827	99	99	99				93	93	93
12	North Simcoe Muskoka	869	870	871	107	108	107				101	101	102
13	North East	916	914	925	133	133	133				83	83	86
14	North West	772	785	792	154	150	150				70	71	71
	Mean	851	851	854	100	100	99				100	100	100
	SD	50.8	48.2	51.6	24.6	23.9	23.8				13.6	13.4	12.7
	CV	6.0	5.7	6.0	24.6	24.0	23.9				13.6	13.4	12.7
	-2 Log Likelihood	3748630	3744757	3628439	814041	811982	798286				1237071	1234478	1202377
	AIC (smaller is better)	3748636	3744769	3628467	814047	811994	798314				1237077	1234490	1202405
	BIC (smaller is better)	3748667	3744773	3628476	814078	811998	798322	58745	58672	58415	1237106	1234494	1202414
	LRT (Chi2 dist, p<0.05)		3872.9	116317.5		2059.4	13696.6		53.0	278.2		2592.5	32100.9

LHIN		Dialysis (50% sample)			Cancer (100% sample)			LTC			CCC			Rehabilitation		
		Obs	RE	Adj	Obs	RE	Adj	Obs	RE	Adj	Obs	RE	Adj	Obs	RE	Adj
	Proportion of zero values (%)	99.9			99.5											
1	Erie St. Clair	-	0.01	0.01	1	1	1									
2	South West	-	0.01	0.01	2	2	2									
3	Waterloo Wellington	0.03	0.05	0.05	15	14	14									
4	Hamilton Niagara	0.22	0.16	0.17	4	4	4									
5	Central West	0.23	0.24	0.24	3	3	3									
6	Mississauga Halton	2.54	2.53	2.52	8	8	8									
7	Toronto Central	-	0.01	0.01	2	2	2									
8	Central	0.08	0.08	0.09	2	2	2									
9	Central East	0.03	0.03	0.03	4	4	4									
10	South East	-	0.01	0.01	3	2	2									
11	Champlain	-	0.01	0.01	2	2	2									
12	North Simcoe Muskoka	0.02	0.03	0.03	2	2	2									
13	North East	-	0.01	0.01	1	1	1									
14	North West	0.95	0.86	0.84	4	3	3									
	Mean	0.29	0.29	0.29	4	4	4									
	SD	0.7	0.7	0.7	3.5	3.5	3.5									
	CV	236.0	237.5	237.0	91.8	92.7	92.8									
	-2 Log Likelihood	7202	6163	5952	67710	63939	62850									
	AIC (smaller is better)	7208	6175	5980	67716	63951	62878									
	BIC (smaller is better)	7240	6178	5989	67750	63955	62887									
	LRT (Chi2 dist, p<0.05)		1039.9	210.3		3771.5	1088.6									

C. Mortality

LHIN		HCU			Non-HCU		
		Obs	RE	Adj	Obs	RE	Adj
	Proportion of zero values (%)						
1	Erie St. Clair	115.7	113.4	113.1	9.8	9.6	9.6
2	South West	106.8	106.4	106.6	9.8	9.7	9.7
3	Waterloo Wellington	118.2	115.1	115.9	8.7	8.6	8.6
4	Hamilton Niagara	109.0	108.5	108.6	8.4	8.4	8.4
5	Central West	97.5	99.1	97.8	5.2	5.5	5.4
6	Mississauga Halton	100.7	101.3	101.4	5.0	5.3	5.3
7	Toronto Central	100.9	101.4	102.2	7.4	7.5	7.5
8	Central	98.3	99.0	99.2	5.5	5.6	5.6
9	Central East	110.6	109.9	110.2	6.8	6.9	6.9
10	South East	106.1	105.7	105.2	8.7	8.6	8.6
11	Champlain	98.6	99.3	99.5	7.6	7.6	7.6
12	North Simcoe Muskoka	103.3	103.5	102.3	8.0	7.9	7.8
13	North East	95.2	97.1	96.1	9.2	9.1	9.0
14	North West	98.1	100.7	100.5	7.9	7.8	7.8
	Mean	104.2	104.3	104.2	7.7	7.7	7.7
	SD	7.1	5.7	6.0	1.6	1.5	1.5
	CV	6.8	5.4	5.7	20.6	18.8	19.1
	-2 Log Likelihood	117793.8	117753.8	112546.6	47190.7	47070.6	44270.4
	AIC (smaller is better)	117795.8	117757.8	112558.6	47192.7	47074.6	44282.4
	BIC (smaller is better)	117805.9	117759.1	112562.4	47203.9	47075.9	44286.2
	LRT (Chi2 dist, p<0.05)		40	5207.2		120.12	2800.21

Appendix 5 **Estimate coefficients, healthcare care expenditures in HCUs, total costs and cost components, incident year**

A: HCU

σ2u1 – variance of the probability of incurring costs; σ2u2 – variance of the costs incurred; R2- coefficient of determination (for part 1 and part 2 of two-part models);

	Total costs			Hospital admission			Physician			Home care			ODB		
	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value
σ2u1				0.022	0.009	0.0297				0.052	0.020	0.0221	0.044	0.020	0.0447
σ2u2	0.001	0.000	0.0264	0.001	0.001	0.0348	0.018	0.007	0.0205	0.007	0.003	0.0232	0.003	0.001	0.0283
Covariance (u1 and u2)				0.003	0.002	0.122				-0.002	0.005	0.6936	0.007	0.004	0.0949
p(costs)=0; Intercept				4.212	0.089	<.0001				-5.310	0.083	<.0001	4.732	0.277	<.0001
Age				-0.028	0.001	<.0001				0.077	0.001	<.0001	-0.023	0.003	<.0001
Sex, M				0.182	0.015	<.0001				-0.387	0.010	<.0001	-0.436	0.054	<.0001
ADG				-0.002	0.002	0.2725				-0.008	0.001	<.0001	0.252	0.007	<.0001
Low – income status				-0.062	0.019	0.0071				0.125	0.014	<.0001	-0.168	0.064	0.023
p(costs)>0; Intercept	9.739	0.019	<.0001	9.170	0.026	<.0001	9.245	0.039	<.0001	6.234	0.038	<.0001	7.925	0.031	<.0001
Age	0.008	0.000	<.0001	0.008	0.000	<.0001	-0.013	0.000	<.0001	0.023	0.000	<.0001	-0.006	0.000	<.0001
Sex, M	0.064	0.003	<.0001	0.125	0.005	<.0001	0.104	0.003	<.0001	-0.053	0.006	<.0001	0.047	0.005	<.0001
ADG	-0.011	0.000	<.0001	-0.020	0.001	<.0001	0.005	0.000	<.0001	-0.002	0.001	0.0306	0.027	0.001	<.0001
Low – income status	0.018	0.004	0.0009	0.022	0.006	0.0031	-0.050	0.004	<.0001	0.037	0.007	0.0004	0.221	0.007	<.0001
log_theta	0.788	0.003	<.0001	0.267	0.003	<.0001	0.969	0.003	<.0001	0.126	0.004	<.0001	-0.113	0.003	<.0001
R2 (part 1)				0.5%			34.5%			10.7%			24.5%		
R2 (part 2)	1.6%			2.2%			4.0%			5.1%			2.3%		

	Emergency department			**Mental health**			**Lab**			**Dialysis**			**Cancer**		
	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value
σ2u1	0.032	0.013	0.0271	0.033	0.016	0.06	0.160	0.061	0.0219	0.392	0.153	0.0248	0.063	0.024	0.0229
σ2u2	0.002	0.001	0.0284	0.018	0.010	0.1064	0.011	0.004	0.0225	0.357	0.141	0.0257	0.020	0.008	0.0257
Covariance (u1 and u2)	0.007	0.003	0.0405	-0.005	0.009	0.6213	0.023	0.013	0.0932	-0.342	0.139	0.0298	-0.034	0.013	0.0263
p(costs)=0; Intercept	-3.015	0.078	<.0001	0.653	0.271	0.0328	1.525	0.130	<.0001	-4.776	0.358	<.0001	2.015	0.112	<.0001
Age	0.051	0.001	<.0001	0.052	0.003	<.0001	-0.007	0.001	<.0001	-0.013	0.004	0.0062	-0.053	0.001	<.0001
Sex, M	0.082	0.011	<.0001	0.271	0.049	0.0001	-0.035	0.014	0.0271	0.557	0.060	<.0001	0.075	0.016	0.0006
ADG	0.022	0.001	<.0001	-0.006	0.006	0.3366	0.082	0.002	<.0001	0.028	0.007	0.0026	-0.020	0.002	<.0001
Low – income status	0.263	0.016	<.0001	-0.231	0.062	0.003	-0.150	0.018	<.0001	0.354	0.073	0.0004	-0.300	0.024	<.0001
p(costs)>0; Intercept	6.404	0.023	<.0001	9.764	0.244	<.0001	4.942	0.035	<.0001	10.667	0.508	<.0001	11.366	0.101	<.0001
Age	0.006	0.000	<.0001	0.007	0.003	0.0484	0.001	0.000	0.0024	-0.005	0.006	0.3919	-0.026	0.001	<.0001
Sex, M	0.031	0.004	<.0001	0.042	0.043	0.3564	0.046	0.004	<.0001	-0.083	0.087	0.3585	0.145	0.016	<.0001
ADG	0.016	0.000	<.0001	-0.017	0.005	0.0038	0.029	0.001	<.0001	-0.039	0.011	0.0035	-0.007	0.002	0.0068
Low – income status	0.046	0.005	<.0001	0.047	0.054	0.4024	0.006	0.005	0.3123	-0.028	0.104	0.7948	-0.115	0.024	0.0005
log_theta	0.810	0.004	<.0001	0.272	0.031	<.0001	0.499	0.003	<.0001	-0.721	0.034	<.0001	-0.069	0.009	<.0001
R2 (part 1)	5.0%			4.6%			3.3%			3.0%			5.7%		
R2 (part 2)	1.7%			1.6%			3.0%			2.9%			4.9%		

	LTC			CCC			Rehabilitation		
	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value
σ2u1	0.044	0.017	0.0262	0.126	0.049	0.0239	0.140	0.054	0.02302
σ2u2	0.001	0.001	0.2826	0.026	0.011	0.0311	0.006	0.003	0.000268
Covariance (u1 and u2)	-0.004	0.003	0.2017	0.001	0.016	0.9579	-0.002	0.008	-0.01988
p(costs)=0; Intercept	-11.062	0.129	<.0001	-8.430	0.159	<.0001	-5.480	0.139	-5.783
Age	0.111	0.001	<.0001	0.072	0.002	<.0001	0.041	0.001	0.03817
Sex, M	-0.412	0.021	<.0001	-0.095	0.024	0.0019	-0.279	0.019	-0.3202
ADG	-0.039	0.003	<.0001	-0.037	0.003	<.0001	-0.022	0.002	-0.0268
Low – income status	0.163	0.023	<.0001	0.059	0.028	0.06	-0.101	0.023	-0.1516
p(costs)>0; Intercept	9.295	0.098	<.0001	9.877	0.131	<.0001	9.322	0.079	9.1486
Age	0.005	0.001	0.001	0.003	0.001	0.0551	0.006	0.001	0.003755
Sex, M	-0.044	0.017	0.0234	-0.001	0.023	0.9624	0.142	0.015	0.1101
ADG	-0.007	0.002	0.0058	-0.008	0.003	0.0126	-0.005	0.002	-0.00834
Low – income status	-0.016	0.018	0.3996	0.032	0.027	0.2505	0.037	0.018	-0.00206
log_theta	0.312	0.012	<.0001	0.028	0.014	0.0695	0.433	0.011	0.4081
R2 (part 1)	19.5%			8.8%			3.7%		
R2 (part 2)	0.5%			0.3%			1.3%		

B Non-HCU

Note: mixed effects models in the following cost categories did not converge among senior non-HCUs: mental health, complex continuing care, long-term care, and rehabilitation services

	Total costs			Hospital admission			Physician			Home care			ODB		
	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value
σ^2_{u1}	0.065	0.026	0.03	0.048	0.019	0.03	0.117	0.046	0.03	0.035	0.014	0.03	0.088	0.034	0.03
σ^2_{u2}	0.001	0.001	0.04	0.003	0.002	0.05	0.014	0.005	0.03	0.015	0.006	0.03	0.002	0.001	0.03
Covariance (u1 and u2)	0.006	0.003	0.06	0.005	0.004	0.17	0.02	0.012	0.13	-0.009	0.007	0.21	0.007	0.004	0.08
p(costs)=0; Intercept	4.49	0.16	<.0001	-1.534	0.086	<.0001	3.639	0.167	<.0001	-13.64	0.096	<.0001	0.694	0.111	<.0001
Age	-0.067	0.002	<.0001	-0.019	0.001	<.0001	-0.057	0.002	<.0001	0.125	0.001	<.0001	-0.023	0.001	<.0001
Sex, M	-0.205	0.03	<.0001	0.254	0.012	<.0001	-0.163	0.029	<.0001	-0.438	0.014	<.0001	-0.192	0.016	<.0001
ADG	1.018	0.009	<.0001	0.125	0.002	<.0001	0.805	0.007	<.0001	0.138	0.002	<.0001	0.556	0.003	<.0001
Low – income status	-0.129	0.035	0.003	-0.179	0.017	<.0001	-0.096	0.034	0.02	0.213	0.016	<.0001	0.041	0.019	0.05
p(costs)>0; Intercept	5.946	0.025	<.0001	6.325	0.046	<.0001	5.719	0.039	<.0001	6.44	0.065	<.0001	5.257	0.029	<.0001
Age	0.016	0.001	<.0001	0.017	0.001	<.0001	0.005	0.001	<.0001	0.013	0.001	<.0001	0.014	0.001	<.0001
Sex, M	0.044	0.005	<.0001	-0.021	0.008	0.02	0.019	0.005	0	-0.092	0.01	<.0001	0.118	0.005	<.0001
ADG	0.081	0.001	<.0001	-0.022	0.002	<.0001	0.074	0.001	<.0001	-0.005	0.002	0	0.055	0.001	<.0001
Low – income status	0.134	0.006	<.0001	0.044	0.012	0	-0.059	0.006	<.0001	0.055	0.011	0	0.424	0.007	<.0001
log_theta	0.473	0.004	<.0001	0.61	0.007	<.0001	0.736	0.004	<.0001	0.543	0.008	<.0001	-0.19	0.003	<.0001
R^2 (part 1)	87.0%			9.8%			79.9%			28.9%			64.9%		
R^2 (part 2)	19.7%			2.7%			17.5%			2.7%			9.2%		

	Emergency department			Lab			Dialysis			Cancer		
	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value	Coeff	SE	P-value
σ2u1	0.092	0.035	0.03	0.073	0.028	0.03	7.305	4.439	0.13	1.325	0.508	0.03
σ2u2	0.002	0.001	0.06	0.008	0.004	0.03	0.547	0.39	0.19	0.305	0.122	0.03
Covariance (u1 and u2)	0.006	0.004	0.14	0.007	0.007	0.37	-1.196	1.22	0.35	-0.583	0.235	0.03
p(costs)=0; Intercept	-3.668	0.102	<.0001	1.185	0.102	<.0001	-12.49	1.169	<.0001	-7.341	0.385	<.0001
Age	0.015	0.001	<.0001	-0.028	0.001	<.0001	0.007	0.01	0.46	-0.003	0.003	0.34
Sex, M	-0.08	0.012	<.0001	-0.052	0.014	0	0.881	0.136	<.0001	0.27	0.042	<.0001
ADG	0.142	0.002	<.0001	0.248	0.002	<.0001	0.169	0.015	<.0001	0.154	0.005	<.0001
Low – income status	0.047	0.016	0.01	-0.008	0.018	0.69	0.898	0.141	<.0001	-0.186	0.061	0.01
p(costs)>0; Intercept	5.259	0.036	<.0001	4.187	0.036	<.0001	5.519	0.628	<.0001	6.827	0.262	<.0001
Age	0.009	0.001	<.0001	0.006	0.001	<.0001	0.009	0.007	0.17	0.004	0.003	0.18
Sex, M	-0.012	0.007	0.09	0.028	0.005	<.0001	-0.04	0.083	0.64	0.032	0.037	0.4
ADG	0.02	0.001	<.0001	0.039	0.001	<.0001	0.004	0.013	0.78	-0.005	0.006	0.35
Low – income status	0.063	0.009	<.0001	0.007	0.007	0.34	-0.009	0.085	0.92	-0.001	0.053	1
log_theta	0.84	0.007	<.0001	0.706	0.005	<.0001	1.039	0.087	<.0001	0.265	0.026	<.0001
R2 (part 1)	10.5%			27.7%			6.8%			8.6%		
R2 (part 2)	3.1%			5.5%			3.1%			0.6%		

Chapter 5

Unplanned Hospitalization among New Senior High Cost Healthcare Users in Ontario, Canada: population-based, matched cohort study

This chapter was submitted to CMAJ Open. It keeps the corresponding format.

Sergei Muratov MD, MPH[1], Justin Lee BScPhm, ACPR, MD, FRCPC[1,2], Anne Holbrook MD, PharmD, MSc, FRCPC[1,3], J Michael Paterson MSc[4,9], Jason R Guertin PhD[5,6], Lawrence Mbuagbaw MD, MPH, PhD, FRSPH[1], Tara Gomes PhD[4,7], Wayne Khuu MPH[4], Priscila Pequeno MSc[4], Jean-Eric Tarride MA, PhD[1,8]

[1]Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada

[2]Division of Geriatric Medicine, Department of Medicine, McMaster University, Hamilton, Ontario, Canada

[3]Division of Clinical Pharmacology and Toxicology, Department of Medicine, McMaster University, Hamilton, Ontario, Canada

[4]ICES, Toronto, Ontario, Canada

[5]Département de médecine sociale et préventive, Faculté de Médecine, Université Laval, Quebec City, Quebec, Canada

[6]Centre de recherche du CHU de Québec, Université Laval, Axe Santé des Populations et Pratiques Optimales en Santé, Québec City, QC, Canada

[7]Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Ontario, Canada

[8]Center for Health Economics and Policy Analysis (CHEPA), McMaster University, Hamilton, Ontario, Canada

[9]Department of Family Medicine, McMaster University, Hamilton, Ontario, Canada

Corresponding author:

Sergei Muratov

Department of Clinical Epidemiology and Biostatistics, McMaster University
1280 Main Street West, Hamilton, ON L8S 4K1

muratos@mcmaster.ca

(905)523-7284

Competing interests: The authors declare that they have no competing interests

Funding and Acknowledgements: This work is supported by in-kind support from the Ontario Drug Policy Research Network (ODPRN) and by personnel awards from the Canadian Institutes of Health Research (CIHR) Drug Safety and Effectiveness Cross-Disciplinary Training (DSECT) Program, the Program for Assessment of Technology in Health (PATH), The Research Institute of St Joe's Hamilton, St Joseph's Healthcare Hamilton, and an Ontario Graduate Scholarship (OGS). The work also is supported by ICES, an independent research institute funded by the Ontario Ministry of Health and Long-Term Care (MOHLTC). ODPRN is funded by grants from the Ontario MOHLTC and the Ontario Strategy for Patient-Orientated Research (SPOR) Support Unit, which is supported by CIHR and the Province of Ontario. The opinions, results, 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. Parts of this material are based on data and information compiled and provided by the Canadian Institute for Health Information (CIHI) and Immigration, Refugees and

Citizenship Canada (IRCC). However, the analyses, conclusions, opinions and statements expressed herein are those of the authors and not necessarily those of CIHI or IRCC.

ABSTRACT

BACKGROUND

Most healthcare spending is concentrated within a relatively small number of high-cost healthcare users (HCU). To inform health policies, we examined the characteristics of index hospitalisations and its predictors among incident senior HCUs compared to non-HCUs in Ontario.

METHODS:

Using Ontario administrative data, incident senior HCUs were identified and matched 1:3 to senior non-HCUs. Senior HCUs were defined as persons aged ≥66 years within the top 5% most costly healthcare users during fiscal year (FY) 2013 but not during FY2012. Index hospitalizations (IHs), the main outcome, were defined as the first unplanned hospital admissions during FY2013 with no hospitalizations in preceding 12 months. Descriptively, we analyzed the attributes of IHs, including IH costs. Predictors of IHs were identified using stratified logistic regression.

RESULTS:

Over half (54.2%) of all HCUs (N=175,847) had an IH compared to 1.7% of non-HCUs (N=527,541). Senior HCUs had a poorer health status, longer acute length of stay (mean, 7.5 vs 2.9 days) and more frequent designation as alternate level of care pre-discharge (20.8% vs. 1.7%). Ten diagnosis codes accounted for one-third of the IH costs. While many predictors were similar across the cohorts, a lower risk of IH among HCUs was associated with residence in long-term care (LTC), attachment to a primary care provider, and recent consultation by a geriatrician.

INTERPRETATION

The high prevalence of IHs and the corresponding costs are a distinctive feature of incident senior HCUs. Improved access to specialist outpatient care, home-based social care, LTC when required are worth further investigation.

Introduction

Most healthcare spending is concentrated within a small group of patients(Wammes et al., 2018). Referred to as the high-cost healthcare users (HCU), the top 5% most costly patients account for 61.1% of all publicly funded healthcare expenditures in Ontario that amounted to $55.9 billion in 2016/2017 ("Expenditure Estimates for the Ministry of Health and Long Term Care (2018-19)," ; Rais et al., 2013). Senior HCUs represent 60% of the overall HCU population(Rais et al., 2013). Since approximately two-thirds of HCU costs are accrued through hospital admissions(Rais et al., 2013; Riley, 2007; Wodchis WP; Wodchis et al., 2016), a detailed examination of hospitalized senior HCUs is warranted.

Currently, there is limited information on several key aspects of senior HCU admissions such as: 1) characteristics of incident HCUs, as opposed to prevalent HCUs, which would allow identification of the factors that influence the transition to HCU status; 2) the first hospital admission, as opposed to re-admission, since the first (or index) hospitalization is the most important predictor of subsequent admissions and of disability in general(Dattalo, Nothelle, & Chapman, 2016; Peikes et al., 2009; Wallace et al., 2014); 3) contribution of individual conditions to the financial burden of hospitalization, which would help programs identify clinical drivers of the highest inpatient expenditures that are potentially divertible by managing risk factors, and 4) outcomes of admission, such as inpatient mortality. Further, although socio-demographic and health attributes of senior HCUs have been reported in Canada and elsewhere(Clough et al., 2016; Holtz-Eakin, 2005; Sinha, 2011; Wammes et al., 2018), little is known about their healthcare prior to the HCU status, especially in Canada, and how these compare to non-HCUs.

Given health care planners' growing concern over the escalating healthcare costs and challenges in managing HCUs(J. Y. Lee et al., 2018), a better characterization of the first unplanned hospitalizations among incident senior HCUs is a timely exercise with important health policy and program implications. The objectives of the study were therefore to describe attributes of the first unplanned hospitalizations in the year of becoming an HCU among incident senior HCUs in comparison with non-HCUs, and to determine predictors of these admissions in both cohorts.

Methods

Design and population

We conducted a retrospective population-based matched cohort study using 2 years of provincial patient data. The 2013 Ontario government fiscal year (April 1, 2013 and March 31, 2014) was considered the incident year (FY2013), while the 2012 fiscal year (FY2012: April 1, 2012 and March 31, 2013) was the baseline or pre-incident year.

FY2013 was the most recent year for which the necessary data were available at the time of study approval.

Incident senior HCUs were defined as individuals aged 66 years or older with annual total healthcare expenditures within the top 5% threshold of all Ontarians in FY2013, who were not in the top 5% in FY2012 fiscal year. The 5% threshold is commonly used in HCU studies in Canada and elsewhere(Guilcher et al., 2016; Holtz-Eakin, 2005; Riley, 2007; Wodchis et al., 2016). Senior non-HCUs were Ontarians in FY2013 with annual total health care expenditures in both FY2012 and FY2013 less than the top 5% threshold. The incident senior HCU cohort was matched with non-HCUs in a ratio of 1:3 according to age at cohort entry (± 1 month), sex and Local Health Integration Network (LHIN) of patient residence. The >66 year age threshold was applied to capture prescription numbers and costs for at least one year before FY2013 as the Ontario Drug Benefits (ODB) eligibility begins at the age of 65.

Data sources

The individual level dataset was created using health administrative databases from Ontario housed at ICES (www.ices.on.ca). These databases contain administrative healthcare service records for all individuals covered by the Ontario Health Insurance Plan (OHIP). Basic demographic information (age, sex, location of residence, vital status) was obtained from the OHIP Registered Persons Database. The health status and comorbidity of the study population was obtained from several sources, including the

Canadian Institute for Health Information's Discharge Abstract Database (DAD), CIHI's National Ambulatory Care Reporting System, ICES-derived and validated cohorts. Health services were captured using the OHIP Claims History Database (physician visits), the Home Care Database (home care visits), the Ontario Drug Benefit Plan Database (prescription drugs), and the CIHI DAD (hospital admissions). More detail regarding these data sources is provided in Appendix 1. Health care expenditures were calculated using ICES person-level costing algorithms based on a costing methodology that links healthcare utilization data from administrative databases and costs collected by the provincial public payer (Wodchis WP et al., 2013). Costs were expressed in 2013 Canadian Dollars. More details on the study design and data sources were published as a study protocol elsewhere (Muratov et al., 2017).

Patient characteristics

The study population was characterized by socio-demographic (e.g., age, sex, income), health status (e.g., Johns Hopkins Aggregate Diagnosis Groups (ADG))(Johns Hopkins ACG® System Version 10.0, 2014), and health care variables (e.g. number of specialist visits) in the baseline year. The variables are briefly summarized in Appendix 1.

Unplanned index hospitalization

Patients with an unplanned index hospitalization (IH), the main outcome, were defined as individuals who had not been hospitalized for at least 12 months prior to their first acute inpatient hospitalization in FY2013. Unplanned IHs were defined as non-elective admissions as recorded in the Discharge Abstract Database. The ICD10-CA diagnosis code most responsible for resource use (further as “diagnosis code”) was used to define the primary reason for each hospitalization. The acute portion of each hospital length of stay (ALOS) was summarized as the mean number of the days of hospitalization. Alternate level of care (ALC) status, which refers to patients who no longer require acute care but who occupy a hospital bed while awaiting placement in another healthcare facility(Sutherland & Crump, 2013), was expressed as the proportion of patients with ALC status. We also calculated the proportion of patients who were admitted to a teaching facility and the proportion who resided in a LHIN different than the hospital LHIN (Appendix 1). IH costs were calculated by diagnosis codes. Inpatient mortality was defined as all-cause in-hospital mortality among the subset of patients who had an unplanned IH. In addition, we calculated the number of days patients were in hospital before death.

Statistical analysis

<u>Descriptive analysis</u>

We first compared the patient characteristics of the two cohorts in FY2012 by measuring absolute standardised difference (aSD). The aSD of 0.1 and above indicated a meaningful difference(Mamdani et al., 2005). In the second step, the attributes of the unplanned IHs among incident senior HCUs versus non-HCUs were described in terms of ALOS, ALC, discharge disposition and death before discharge. Thirdly, the most common clinical causes of admission and their associated costs were determined for both groups. The cumulative percentage of the total unplanned IH costs by diagnosis codes and average annual costs for each diagnosis were also computed.

Predictive analysis

We used logistic regression, one model for each cohort, to identify independent predictors of unplanned IHs. For each model, an IH event was the binary dependent variable. The list of potential predictors (independent variables) consisted of socio-demographic, health status and healthcare characteristics measured in FY2012 that are described under the corresponding sections of Appendix 1. Odds ratios and 95% confidence intervals were reported. We included all relevant variables in the models regardless of their statistical significance. We assessed model discrimination using the c-statistic, where a c-statistic value of 0.70 and above indicates good discrimination (Hosmer DW & Lemeshow S, 2000). We evaluated the model's ability to predict subgroups of patients with a differing risk of index hospitalization (Kramer & Zimmerman, 2007; Pocock et al., 2006) and each model was validated through cross-validation ("ROC analysis using validation data and cross validation. SAS Support. © SAS Institute Inc.,") and checked for multicollinearity. Additional information on the statistical methods is provided in Appendices 2-3.

Ethics Approval

This study was approved by Hamilton Integrated Research Ethics Board (ID#1715-C).

Results

Baseline patient characteristics

The total study population consisted of 703,388 seniors, of which 175,847 were incident HCUs. The average age was 77.7 years and 53% of individuals in both cohorts were women and resided in suburban areas (Table 1). Compared to non-HCUs, senior HCUs were sicker (number of ADGs: 10.2 vs. 7.9%, aSD=0.54), were dispensed a higher number of medications (8.4 vs 5.6, aSD=0.6), visited their primary care provider more often (95.6% vs. 84.3%, aSD=0.38), received more specialty care (89.8% vs. 74.2%; aSD=0.41) and home care services in the year preceding the index year. Senior HCUs were more likely to have a primary care provider (primary care group: 97% vs. 88.6%, aSD=0.33). More than one third of the senior HCUs visited an emergency department compared to non-HCUs (31.8% vs. 19.3%, aSD=0.29). The non-HCUs had a higher proportion of recent immigrants (4.3% vs. 2.4%; aSD=0.11). In terms of the other study characteristics, the study cohorts were otherwise similar.

Characteristics of unplanned index hospitalization

Unplanned IHs accounted for 71% and 82% of index hospitalizations among senior HCUs and non-HCUs, respectively. More than half of the HCUs (N=95,308; 54.2%) had an unplanned IH compared to only 1.7% (N=8,835) of the non-HCUs (Table 2). Among those hospitalized, senior HCUs had a longer length of stay (mean ALOS, 7.5 vs 2.9 days; aSD=0.73), were designated ALC status in higher numbers (20.8% vs. 1.7%; aSD=64), and, once transferred to ALC, had a relatively greater number of ALC days (2.96 vs. 0.06 days; aSD=0.32). Compared with 1.3% of non-HCUs, 23.0% of senior HCU patients were transferred to another acute care or LTC facility, while most non-HCU seniors (83.6%) were discharged home (with or without support). There was a striking difference in inpatient mortality between the cohorts: non-HCU patients were more than twice as likely to die in hospital compared to senior HCUs (14.0% vs. 6.4%, aSD=0.25), despite the HCUs longer mean ALOS. Among those who died in hospital, non-HCUs also had a substantially shorter stay before death (2.3 vs. 17.9 days; aSD=1.92).

Index hospitalization costs

Unplanned IHs accounted for 74% (HCU) and 81% (non-HCU) of the costs associated with all IH (unplanned plus elective) during the year of study. The average cost per patient associated with the unplanned IH was $12,471 (SD $19,935) for senior HCUs and $3,749 (SD: $1,290) for non HCU (Table 3). Ten conditions accounted for one third of the costs: 36.4% (HCU) and 35.3% (non-HCU). Acute myocardial infarction (8%) was the leading most costly reason of IH among HCUs, compared to pneumonia (6%) among non-HCUs. Five conditions (i.e., cerebral infarction, congestive heart failure (HF), pneumonia, chronic obstructive pulmonary disease (COPD), and ileus/intestinal obstruction) were among the top 10 most costly conditions in both cohorts. The costliest conditions were also the most frequent causes of unplanned hospitalizations in both cohorts.

Predictors of unplanned IHs

Overall, the direction, magnitude and significance of odds ratios (OR) were similar across the two cohorts for many of the predictors of unplanned IH (Table 4). Predictors specific to the HCU cohort included having visited a geriatrician in the previous year and living at long-term care facilities. Both were associated with lower odds of IHs (ORs: 0.81, 95%CIs 0.76-0.86 and 0.29, 95%CIs 0.25-0.34, respectively). Recent immigrants had lower odds of IHs which was unique among senior non-HCUs (ORs: 0.72, 95% CIs 0.62-0.84). In contrast to many predictors with a low magnitude of association, the "other" category of home care services for senior HCUs had a non-negligible protective effect in IHs (ORs: 0.94, 95% CIs 0.93-0.94). Since this variable was constructed to include a combination of social services, respite care and case management, it was impossible to tease out the impact of each of these services alone. Finally, incident senior HCUs who had a primary care provider were at a lower risk of admission whereas among non-HCUs, attachment to a provider was associated with an increase in IH. This fact may allude to the existence of subgroups of 'orphan' patients that differ based on severity of illness, personality type, social circumstance or, among HCUs, access to primary care(Hay, Pacey, Bains, & Ardal, 2010).

Interpretation

Our study provides an analysis of high cost healthcare use amongst seniors in Ontario. By examining the first hospitalization among "new" cases of senior HCUs in comparison with age, sex and geographically-matched non-HCUs, we found that unplanned HIs were much more common among high cost seniors, with more than a half of incident senior HCUs having an unplanned IH compared to less than 2% of non-HCUs. Ten conditions, many of which have known remediable risk factors of hospitalization(An, Kim, & Yoon, 2017; Del Gobbo et al., 2015; Lim & Kwon, 2010; Woolf & Åkesson, 2003; Yusuf et al., 2004), accounted for a large number of these admissions and one third of their costs.

Besides a greater admission rate, incident senior HCUs had longer hospital stays and were frequently designated as ALC. Also, compared to senior non-HCUs, HCUs who died in hospital stayed there for weeks on average prior to death suggesting a prolonged terminal phase. Finally, our findings indicate that despite a few predictors (e.g., visits to a geriatrician or attachment to a primary care provider) were unique to each cohort, there were many similarities in baseline predictors of the first unplanned admission between the two cohorts, including healthcare received prior to the incident year.

Any comparison of our results with other studies is challenging due to methodological heterogeneity: e.g., the lack of differentiation between the category of admission (unplanned vs. elective), inclusion of re-admissions, or the use of a different HCU threshold (e.g., top 1%). However, we found our results to be consistent with previous research in several aspects. First, our list of the most frequent and most costly disease codes is overall in line with prior limited studies on senior HCUs from Canada and elsewhere that examined the financial contribution of individual conditions: cardio-vascular, orthopedic, infectious diseases are predominant reasons of admissions(K. E. Joynt, Gawande, Orav, & Jha, 2013; Wodchis et al., 2016). Further, a number of models from different jurisdictions examined this risk among community-dwelling seniors(Wallace et al., 2014). Similar to our results, older age, male sex, visits to the ED and prevalent chronic conditions were associated with higher odds of admission. Our findings support earlier reports of the “healthy immigrant” effect(Vang, Sigouin, Flenon, & Gagnon, 2017): recent senior immigrants were less likely to become HCUs or be admitted with an IH. In contrast to previous studies of the general senior population that suggested residence at a nursing home be a predictor of future admissions, especially for fracture(Graverholt et al., 2011; Ronald, McGregor, McGrail, Tate, & Broemling, 2008), living in a LTC facility was associated with lower risk for unplanned IHs among incident senior HCUs.

Limitations

Key strengths of this study include its population-based, matched design, and our examination of poorly studied aspects of the senior HCU population in the Canadian context. Our study also has limitations. The discriminatory power of the models was only fair, although the values of c-statistic were close to a number of previously reported risk prediction models in the general senior population(Wallace et al., 2014). Running the models on more homogeneous subgroups of patients (e.g. COPD, HF) improved model discrimination (e.g. c-statistics above .7), especially for HCUs (Appendix 4), and these results were consistent with the main analyses. Further, some findings are based on variables with low prevalence: LTC residence status (n=835; 0.5%), geriatrician visits (n=4967; 2.8%), although this is relative to the very large size of the study population. The study focused only on unplanned IHs rather than including elective admissions. This limits the generalizability of our results to all hospitalizations, but unplanned admissions account for >70% in either cohort. Finally, our modeling is exploratory - the results suggest association but certainly not causation.

Conclusions

The high prevalence of IH and the corresponding costs driven partly by longer lengths of stay for acute care and more ALC are a distinctive feature of incident senior HCUs. The effect of Improved access to specialist outpatient care, home-based social care, and LTC when required, warrant further research.

References

1. Wammes JJG, van der Wees PJ, Tanke MAC, Westert GP, Jeurissen PPT. Systematic review of high-cost patients' characteristics and healthcare utilisation. BMJ Open. 2018;8(9):e023113.
2. Rais S, Nazerian A, Ardal S, Chechulin Y, Bains N, Malikov K. High-cost users of Ontario's healthcare services. Healthcare policy = Politiques de sante. 2013;9(1):44-51.
3. Expenditure Estimates for the Ministry of Health and Long Term Care (2018-19) [Available from: https://www.ontario.ca/page/expenditure-estimates-ministry-health-and-long-term-care-2018-19.
4. Wodchis WP. The Concentration of Health Care Spending: Little Ado (yet) About Much (money). Presented at the Canadian Association for Health Services and Policy Research (CASHPR) 2012 Conference. Available at: https://www.cahspr.ca/web/uploads/presentations/C6.1_Walter_P._Wodchis.pdf. Accessed October 1, 2015.
5. Riley GF. Long-term trends in the concentration of Medicare spending. Health affairs (Project Hope). 2007;26(3):808-16.
6. Wodchis WP, Austin PC, Henry DA. A 3-year study of high-cost users of health care. Cmaj. 2016;188(3):182-8.
7. Peikes D, Chen A, Schore J, Brown R. Effects of care coordination on hospitalization, quality of care, and health care expenditures among Medicare beneficiaries: 15 randomized trials. Jama. 2009;301(6):603-18.
8. Dattalo M, Nothelle S, Chapman EN. Targeting Enhanced Services Toward High-Cost, High-Need Medicare Patients. New Directions in Geriatric Medicine Concepts, Trends, and Evidence-Based Practice 2016. p. 13-30.
9. Wallace E, Stuart E, Vaughan N, Bennett K, Fahey T, Smith SM. Risk prediction models to predict emergency hospital admission in community-dwelling adults: a systematic review. Medical care. 2014;52(8):751-65.
10. Holtz-Eakin D. High-Cost Medicare Beneficiaries 2005 [Available from: http://www.cbo.gov/publication/16487
11. Sinha SK. Why the elderly could bankrupt Canada and how demographic imperatives will force the redesign of acute care service delivery. HealthcarePapers. 2011;11(1):46-51; discussion 86-91.
12. Clough JD, Riley GF, Cohen M, Hanley SM, Sanghavi D, DeWalt DA, et al. Patterns of care for clinically distinct segments of high cost Medicare beneficiaries. Healthcare (Amsterdam, Netherlands). 2016;4(3):160-5.
13. Lee JY, Muratov S, Tarride JE, Holbrook AM. Managing High-Cost Healthcare Users: The International Search for Effective Evidence-Supported Strategies. J Am Geriatr Soc. 2018.
14. Guilcher SJ, Bronskill SE, Guan J, Wodchis WP. Who Are the High-Cost Users? A Method for Person-Centred Attribution of Health Care Spending. PLoS One. 2016;11(3):e0149179.
15. Wodchis WP, Bushmeneva K, Nikitovic M, McKillop I. Guidelines on Person-Level Costing Using Administrative Databases in Ontario. Toronto: Health System Performance Research Network; 2013.
16. Muratov S, Lee J, Holbrook A, Paterson JM, Guertin JR, Mbuagbaw L, et al. Senior high-cost healthcare users' resource utilization and outcomes: a protocol of a retrospective matched cohort study in Canada. BMJ Open. 2017;7(12):e018488.

17. Johns Hopkins ACG® System Version 10.0. Technical Reference Guide: Department of Health Policy and Management, Johns Hopkins University, Bloomberg School of Public Health; 2014 [
18. Sutherland JM, Crump RT. Alternative level of care: Canada's hospital beds, the evidence and options. Healthcare policy = Politiques de sante. 2013;9(1):26-34.
19. Mamdani M, Sykora K, Li P, Normand S-LT, Streiner DL, Austin PC, et al. Reader's guide to critical appraisal of cohort studies: 2. Assessing potential for confounding. BMJ : British Medical Journal. 2005;330(7497):960-2.
20. Hosmer DW, Lemeshow S. Applied Logistic Regression (2nd Edition). New York, NY: John Wiley & Sons; 2000.
21. Kramer AA, Zimmerman JE. Assessing the calibration of mortality benchmarks in critical care: The Hosmer-Lemeshow test revisited. Critical care medicine. 2007;35(9):2052-6.
22. Pocock SJ, Wang D, Pfeffer MA, Yusuf S, McMurray JJ, Swedberg KB, et al. Predictors of mortality and morbidity in patients with chronic heart failure. European heart journal. 2006;27(1):65-75.
23. ROC analysis using validation data and cross validation. SAS Support. © SAS Institute Inc. [Available from: http://support.sas.com/kb/39/724.html.
24. Hay C, Pacey M, Bains N, Ardal S. Understanding the Unattached Population in Ontario: Evidence from the Primary Care Access Survey (PCAS). Healthcare policy = Politiques de sante. 2010;6(2):33-47.
25. An SJ, Kim TJ, Yoon BW. Epidemiology, Risk Factors, and Clinical Features of Intracerebral Hemorrhage: An Update. Journal of stroke. 2017;19(1):3-10.
26. Del Gobbo LC, Kalantarian S, Imamura F, Lemaitre R, Siscovick DS, Psaty BM, et al. Contribution of Major Lifestyle Risk Factors for Incident Heart Failure in Older Adults: The Cardiovascular Health Study. Jacc Heart Failure. 2015;3(7):520-8.
27. Lim J-S, Kwon H-M. Risk of "silent stroke" in patients older than 60 years: risk assessment and clinical perspectives. Clinical Interventions in Aging. 2010;5:239-51.
28. Woolf AD, Åkesson K. Preventing fractures in elderly people. BMJ : British Medical Journal. 2003;327(7406):89-95.
29. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet (London, England). 2004;364(9438):937-52.
30. Joynt KE, Gawande AA, Orav EJ, Jha AK. Contribution of preventable acute care spending to total spending for high-cost Medicare patients. JAMA. 2013;309(24):2572-8.
31. Vang ZM, Sigouin J, Flenon A, Gagnon A. Are immigrants healthier than native-born Canadians? A systematic review of the healthy immigrant effect in Canada. Ethnicity & health. 2017;22(3):209-41.
32. Graverholt B, Riise T, Jamtvedt G, Ranhoff AH, Kruger K, Nortvedt MW. Acute hospital admissions among nursing home residents: a population-based observational study. BMC Health Serv Res. 2011;11:126.
33. Ronald LA, McGregor MJ, McGrail KM, Tate RB, Broemling AM. Hospitalization rates of nursing home residents and community-dwelling seniors in British Columbia. Canadian journal on aging = La revue canadienne du vieillissement. 2008;27(1):109-15.

Table 1: Characteristics of HCU Study Population in the Pre-incident Year

Characteristic		HCU (N=175,847)	Non-HCU (N=527,541)	aSD
Socio-demographics				
Age, mean ± SD, yr		77.66 ± 7.65	77.66 ± 7.65	0
Sex, female, #/yr (%/yr)		93,119 (53%)	279,501 (53.0%)	0
Rural Index of Ontario (RIO) score[a], mean ± SD		12.23 ± 18.20	11.81 ± 18.18	0.02
Low income, #/yr (%/yr)		31,843 (18.1%)	92,566 (17.5%)	0.01
Recent immigrant (<15 yr in Canada), #/yr (%/yr)		4,210 (2.4%)	22,577 (4.3%)	0.11
Health Status				
# Adjusted Diagnostic Groups, mean ± SD		10.22 ± 4.00	7.93 ± 4.47	0.54
Hypertension, #/yr (%/yr)[b]		110,692 (63.0%)	282,867 (53.6%)	0.19
Congestive Heart Failure, #/yr (%/yr)[c]		25,195 (14.3%)	36,877 (7.0%)	0.24
Chronic Obstructive Disease Pulmonary, #/yr (%/yr)[c]		48,738 (27.7%)	96,513 (18.3%)	0.23
Diabetes, #/yr (%/yr)[c]		62,014 (35.3%)	138,794 (26.3%)	0.2
Myocardial infarction, #/yr (%/yr)[c]		12,892 (7.3%)	24,024 (4.6%)	0.12
Rheumatoid Arthritis, #/yr (%/yr)[c]		5,607 (3.2%)	9,334 (1.8%)	0.09
Malignancy, #/yr (%/yr)[b]		56,855 (32.3%)	123,932 (23.5%)	0.2
Mental Health condition, #/yr (%/yr)[b]		67,441 (38.4%)	144,377 (27.4%)	0.24
Health Care utilization				
Long-term care facility, #/yr (%/yr)		835 (0.5%)	316 (0.1%)	0.08
Primary care provider enrollment model, #/yr (%/yr)				
	Fee for service	16,938 (9.6%)	45,751 (8.7%)	0.03
	Capitation	48,703 (27.7%)	133,915 (25.4%)	0.05
	Enhanced fee for service	51,637 (29.4%)	143,940 (27.3%)	0.05
	Family Health Team	51,159 (29.1%)	137,516 (26.1%)	0.07
	None (no primary care provider identified)	5,187 (3.0%)	60,170 (11.4%)	0.33
Number of medications, mean ± SD		8.44 ± 4.96	5.61 ± 4.47	0.6
Emergency department visits (%/yr)	#/yr	55,964 (31.8%)	101,896 (19.3%)	0.29
	mean ± SD	0.56 ± 1.13	0.30 ± 0.80	0.26
Visits to a general practitioner (%/yr)	#/yr	168,024 (95.6%)	444,614 (84.3%)	0.38
	mean ± SD	8.03 ± 6.79	5.63 ± 5.58	0.39
Visits to a specialist (%/yr)	#/yr	157,823 (89.8%)	391,557 (74.2%)	0.41
	mean ± SD	7.40 ± 6.65	4.43 ± 5.13	0.5
Visits to a geriatrician		4,967 (2.8%)	5,935 (1.1%)	0.12
Homecare visits				
Nursing (%/yr)	#/yr	7,218 (4.1%)	7,385 (1.4%)	0.17
	mean ± SD	0.54 ± 4.03	0.16 ± 2.00	0.12
Personal support (%/yr)	#/yr	13,789 (7.8%)	10,612 (2.0%)	0.27
	mean ± SD	6.43 ± 30.57	1.46 ± 13.53	0.21

Allied health (%/yr)	#/yr	9,250 (5.3%)	7,982 (1.5%)	0.21
	mean ± SD	0.18 ± 0.99	0.05 ± 0.52	0.17
Other[e] (%/yr)	#/yr	27,605 (15.7%)	25,965 (4.9%)	0.36
	mean ± SD	0.58 ± 2.30	0.14 ± 0.96	0.25

a- RIO score classification: urban= <10; suburban=10-39; rural ≥40

b- constructed based on Expanded Diagnosis Codes; c- ICES-derived cohort; d- a mean of care utilization refers to the number per person per FY2012;

e - included a combination of social support, respite care, and case management;

aSD- absolute standardized difference with aSD > 0.1 indicating meaningful difference between admitted and non-admitted; SD- standard deviation

Table 2: Characteristics of unplanned index hospitalizations*

Characteristic	HCU	Non-HCU	aSD
Number of individuals with an IH (% of total population)	133,821 (76%)	10,770 (2%)	
Number of individuals with an unplanned IHs (% of total patient with IH)	95,308 (71%)	8,835 (82%)	
Acute length of stay, mean ± SD, days	7.52 ± 8.71	2.91 ± 2.16	0.73
Alternate level of care# (ALC)	19,849 (20.8%)	147 (1.7%)	0.64
# days spent in ALC (for those with ALC designation), mean ± SD	2.96 ± 12.71	0.06 ± 0.72	0.32
Discharge disposition			
Inpatient hospital care	6,279 (6.6%)	47 (0.5%)	0.33
Long term or continuing care facility	15,602 (16.4%)	70 (0.8%)	0.58
Home with support§	23,810 (25.0%)	1,097 (12.4%)	0.33
Home	42,994 (45.1%)	6,293 (71.2%)	0.55
Admission to a teaching care facility	25,597 (26.9%)	2,097 (23.7%)	0.07
Admission to an out of health district acute care facility	10,390 (10.9%)	770 (8.7%)	0.07
Death before discharge	6,112 (6.4%)	1,241 (14.0%)	0.25
Number of days spent at the hospital before death outcome	17.86 ± 25.27	2.32 ± 1.85	0.87

*- defined as first admission in the incident year among those without hospitalization in the past 12 months

- refers to seniors that no longer require acute care but occupy hospital beds waiting for placement in other healthcare facilities

§-support options include: senior's lodge, attendant care, home care, meals on wheels, homemaking, supportive housing, etc

SD- standard deviation; aSD- absolute standardized difference with aSD > 0.1 indicating meaningful difference between women and men

Table 3: Top 20 most expensive conditions, unplanned index hospitalization (IH)

	HCU, n (IH)= 95,308 Total 1-year inpatient cost associated with unplanned IHs: $1,188,544,347 (74% of all HCU hospitalizations) Average costs per HCU (mean ± SD): 12,471 ± 19,935							Non-HCU, n (IH)= 8,835 Total 1-eyar inpatient costs associated with unplanned IHs: $33,130,373 (81% of all non-HCU hospitalizations) Average costs per non-HCU (mean ± SD): 3,749 ± 1,290					
	ICD10 code	Condition	Inpatient costs	Frequency (%)	Average cost	Cumulative to total unplanned costs		ICD10 code	Condition	Inpatient costs	Frequency (%)	Average cost	Cumulative to total unplanned costs
1	I21	Acute myocardial infarction	$ 92,924,331	6045 (6.3)	$ 15,372	7.8%		J18	Pneumonia	$ 1,970,229	439 (5)	$ 4,488	6%
2	S72	Fracture of femur	$ 84,898,511	5181 (5.4)	$ 16,387	15.0%		J44	Chronic obstructive pulmonary disease	$ 1,448,358	304 (3.4)	$ 4,764	10.3%
3	I63	Cerebral infarction	$ 54,321,115	3912 (4.1)	$ 13,886	19.5%		R55	Syncope and collapse	$ 1,337,334	432 (4.9)	$ 3,096	14.4%
4	I50	Heart failure	$ 41,778,511	4069 (4.3)	$ 10,268	23.0%		I48	Atrial fibrillation and flutter	$ 1,120,051	316 (3.6)	$ 3,544	17.7%
5	J44	Chronic obstructive pulmonary disease	$ 37,347,675	4184 (4.4)	$ 8,926	26.2%		N39	Disorders of urinary system	$ 1,115,864	267 (3)	$ 4,179	21.1%
6	A41	Septicaemia	$ 31,204,568	1487 (1.6)	$ 20,985	28.8%		I50	Heart failure	$ 1,114,152	235 (2.7)	$ 4,741	24.5%
7	J18	Pneumonia	$ 25,734,867	2811 (2.9)	$ 9,155	31.0%		R07	Pain in throat and chest	$ 1,040,653	373 (4.2)	$ 2,789	27.6%
8	I25	Chronic ischaemic heart disease	$ 25,625,722	1352 (1.4)	$ 18,954	33.1%		K56	Paralytic ileus and intestinal obstruction	$ 887,673	266 (3)	$ 3,337	30.3%
9	F05	Delirium, not induced by alcohol and other psychoactive substances	$ 20,132,341	1305 (1.4)	$ 15,427	34.8%		I63	Cerebral infarction	$ 834,442	153 (1.7)	$ 5,454	32.8%
10	K56	Paralytic ileus and intestinal obstruction without hernia	$ 19,169,069	1501 ()	$ 12,771	36.4%		Z51	Other medical care	$ 818,228	266 (3)	$ 3,076	35.3%
	64 ICD10codes account for 75% of the total unplanned IH costs							53 ICD10codes account for 75% of the total unplanned IH costs					
	852 ICD10codes account for 100% of the total unplanned IH costs							435 ICD10codes account for 100% of the total unplanned IH costs					

Table 4 Predictors of unplanned index hospitalization

Covariates		HCUs OR (95% CI)	P value	Non-HCUs OR (95% CI)	P value
Age:					
	75-84y **vs.** 66-74y	1.33 (1.29-1.37)	<.0001	1.5 (1.42-1.58)	<.0001
	>=85y vs. 66-74y	1.66 (1.6-1.71)	<.0001	2.53 (2.39-2.69)	<.0001
Sex (M)		1.03 (1.01-1.06)	0.0081	1.06 (1.01-1.1)	0.0167
Low income status		1.04 (1.01-1.08)	0.013	1.06 (1-1.12)	0.0359
Rurality Index for Ontario, score		1 (1-1)	0.7553	1.01 (1.01-1.01)	<.0001
Immigrant status		0.98 (0.9-1.05)	0.5213	0.72 (0.62-0.84)	<.0001
Malignancy		0.81 (0.79-0.83)	<.0001	1 (0.95-1.05)	0.9556
Hypertension		1.09 (1.06-1.12)	<.0001	1.08 (1.03-1.13)	0.0015
Congestive heart failure (CHF)		1.36 (1.32-1.41)	<.0001	1.47 (1.37-1.57)	<.0001
History of myocardial infarction		1.21 (1.16-1.27)	<.0001	1.43 (1.32-1.55)	<.0001
Chronic Obstructive Pulmonary Disease (COPD)		1.26 (1.22-1.29)	<.0001	1.27 (1.21-1.34)	<.0001
Diabetes		0.93 (0.91-0.96)	<.0001	0.95 (0.9-1)	0.0485
Rheumatoid arthritis		1.09 (1.02-1.16)	0.0111	1.08 (0.93-1.25)	0.3401
Mental health condition		0.98 (0.96-1.01)	0.113	1.09 (1.04-1.14)	0.0004
LTC residence		0.29 (0.25-0.34)	<.0001	1.13 (0.58-2.21)	0.7235
Primary care enrollment					
	FFS vs. no provider	0.83 (0.77-0.91)	<.0001	3.64 (3.18-4.17)	<.0001
	Capitation vs. no provider	0.75 (0.7-0.82)	<.0001	3.14 (2.77-3.55)	<.0001
	Enhanced FFS vs. no provider	0.78 (0.72-0.84)	<.0001	2.99 (2.64-3.39)	<.0001
	FHT vs. no provider	0.79 (0.73-0.85)	<.0001	3.65 (3.23-4.13)	<.0001
Prescription drugs		0.99 (0.98-0.99)	<.0001	1.01 (1.01-1.02)	0.0001
Emergency department visits		1.06 (1.05-1.08)	<.0001	1.16 (1.14-1.18)	<.0001
Visits to general practitioner		1 (0.99-1)	<.0001	1 (0.99-1)	0.2336
Visits to specialist		0.95 (0.95-0.95)	<.0001	0.99 (0.99-1)	0.0035
Visit to a geriatrician		0.81 (0.76-0.86)	<.0001	1.06 (0.89-1.26)	0.5223
Homecare visits					
	nursing	0.99 (0.99-1)	<.0001	1.01 (1-1.01)	0.1919
	personal support	1 (1-1)	<.0001	1 (0.99-1)	<.0001
	allied health	1.01 (1-1.02)	0.2753	1.01 (0.98-1.05)	0.4088
	other	0.94 (0.93-0.94)	<.0001	1.02 (1.01-1.04)	0.0007
C-statistics		0.65		0.67	
C-statistics (cross-validated)		0.65		0.67	

Note: See Appendix 5 for detail on predictive accuracy

COPD- Chronic Obstructive Pulmonary Disease (COPD), CHF- Congestive heart failure (CHF), FFS- fee for service, LTC- long-term care

Appendix 1 Description of independent predictors

Key variables	Type of variable	Description	Data source
Demographics (baseline year, FY2012)			
Age	Continuous	Age in years	RPDB
Sex	Categorical (binary)	Sex; female or male	RPDB
Rio2008	Continuous	Rurality Index for Ontario; on a scale of 0 to 100 with 100 being most rural	RPDB
Lowinc	Categorical (binary)	Subjects with low income status were identified based upon net household income reported to receive public drug benefit subsidy in FY2012 which relies on actual net income. For a small proportion of HCU (3%) and non-HCU (13%) who did not fill a prescription in FY2012, low-income status was defined as census neighborhood income quintile	ODB
Recent_immigration	Categorical (binary)	Whether immigrated in 15 years prior to FY2012 (based on landing records for permanent legal immigrants in Ontario)	CIC
Health status/comorbidity (baseline year, FY2012)			
# of ADGs	Continuous	Aggregated Diagnosis Groups (ADGs) are derived from Johns Hopkins Adjusted Clinical Groups (ACGs, the Johns Hopkins ACG® System Version 10): a person-focused, diagnosis-based way to measure patients' illness	DAD, NACRS, OHIP
Hypertension, Malignancy, Mental health condition	Categorical (binary)	For each condition, whether the patient was diagnosed with the condition in the past 3 years prior to FY2013; computed using John Hopkins Expanded Diagnosis Clusters (EDCs)	DAD, NACRS, OHIP
Congestive heart failure, History of myocardial infarction, Chronic Obstructive Pulmonary Disease, Diabetes, Rheumatoid arthritis	Categorical (binary)	Whether the patient is listed in a corresponding ICES-derived cohort for each condition	CHF, COPD, ODD, OMID, ORAD
Healthcare characteristics (baseline year, FY2012)			
# of drugnames	Continuous	Number of prescription drugs the patient was dispensed	ODB
# of physician visits	Continuous	Number of physician visits; reported by categories (family practitioner and specialist)	OHIP
# of home care visits	Continuous	Number of home care visits; reported as total and by categories (nursing, personal support, allied health and other)	HCD
Geriatrician	Categorical (binary)	Whether visited a geriatrician	OHIP
Primarycare group	Categorical	Primary care payment models: Fee for Service (FFS), Enhanced FFS, Family Health Team (FHT), Capitation, and None	CAPE
Long-term care (LTC)	Categorical (binary)	Whether was placed in a LTC facility	ODB
Features of Index hospitalizations (incident year, FY2013)			
LOS	Continuous	Length of stay, days	DAD
instftyp_	Categorical	Institution from where admitted	DAD
instlhin_	Categorical	LHIN where admitted	DAD
dx10code1-25	Character	Diagnosis ICD10 codes for each admission	DAD
dischdisp	Categorical	Institution where discharged to	DAD

inpatient_costs_	Continuous	Inpatient hospitalization Costs	DAD

CAPE - Client Agency Program Enrolment, ICES-derived (Congestive Heart Failure (CHF) database; Chronic Obstructive Pulmonary Disease (COPD) database; Ontario Diabetes Database (ODD); Ontario Myocardial Infarction Database (OMID); and the Ontario Rheumatoid Arthritis Database (ORAD)); CIC - Citizenship and Immigration Canada; DAD – Discharge Abstract Database; NACRS - National Ambulatory Care Reporting System; HCD - Ontario Home Care Database; ODB – Ontario Drug Benefit; OHIP - Ontario Health Insurance Plan; RPDB - Ontario Registered Persons Database

Appendix 2: Supplemental statistical and sensitivity analysis section

Model discrimination (predictive accuracy) was assessed by the area under the receiver operating characteristic curve (AUROC) represented by the c-statistic. We used a threshold of a c-statistic value of 0.70 and above indicates good discrimination between those admitted versus not admitted(Hosmer DW & Lemeshow S, 2000). We evaluated the model's ability to predict subgroups of patients with a differing risk of index hospitalization by plotting predicted vs. observed events in deciles(Kramer & Zimmerman, 2007; Pocock et al., 2006). Each model was validated through cross-validation ("ROC analysis using validation data and cross validation. SAS Support. © SAS Institute Inc.,").

As a check for collinearity, we also re-ran each multivariable model using the forward stepwise procedure with p-value <0.1 set as the inclusion criterion and p-value >0.05 as the removal threshold. We then compared the final selection of variables, the sign and magnitude of the odds ratios (OR) as well as their standard errors (SE): no discrepancy with the original results provided further evidence of a good fit and no/low collinearity. The results of the stepwise approach were closely aligned with the original models (data available from the authors on request).

We also re-ran the models individually on 5 most costly conditions in both cohorts: the predictor estimates remained unaffected while c-statistics improved to above 0.7, especially among HCUs (Appendix 4).

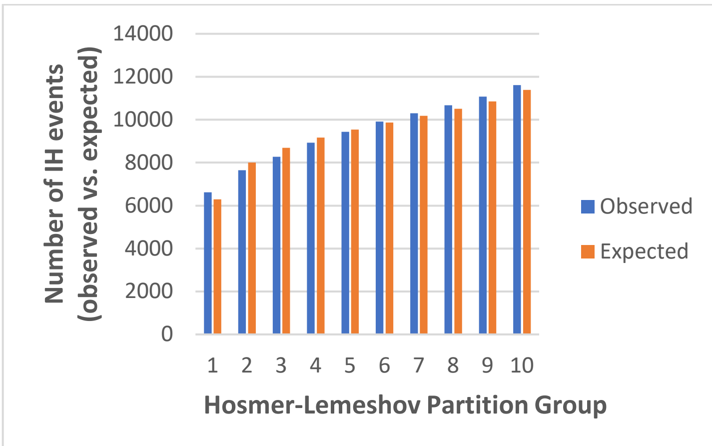
1. Hosmer DW, Lemeshow S. Applied Logistic Regression (2nd Edition). New York, NY: John Wiley & Sons; 2000.

2. Kramer AA, Zimmerman JE. Assessing the calibration of mortality benchmarks in critical care: The Hosmer-Lemeshow test revisited. Critical care medicine. 2007;35(9):2052-6.
3. Pocock SJ, Wang D, Pfeffer MA, Yusuf S, McMurray JJ, Swedberg KB, et al. Predictors of mortality and morbidity in patients with chronic heart failure. European heart journal. 2006;27(1):65-75.
4. ROC analysis using validation data and cross validation. SAS Support. © SAS Institute Inc. [Available from: http://support.sas.com/kb/39/724.html.
5. Clark D, Armstrong M, Allan A, Graham F, Carnon A, Isles C. Imminence of death among hospital inpatients: Prevalent cohort study. Palliative medicine. 2014;28(6):474-9.

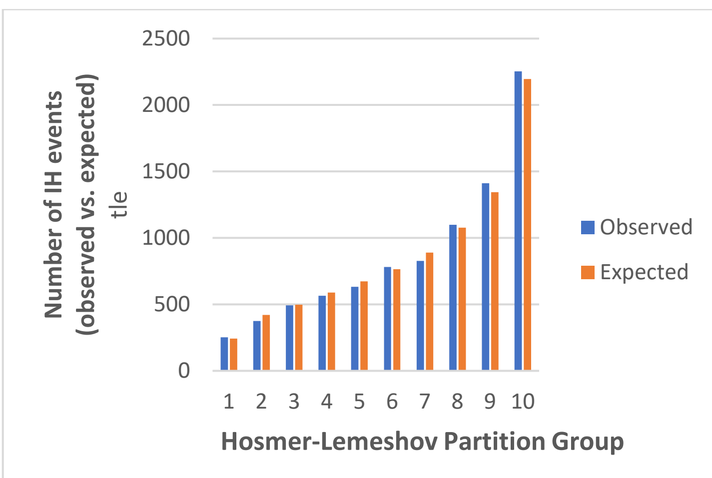
Appendix 3: Predictive accuracy of the models

The models were able to predict the number of events (i.e., IHs) for subgroups of patients with a high degree of accuracy according to the plots below. This supports a good fit of the models.

A. Index hospitalization – HCU



B. Index hospitalization – non-HCU



Appendix 4: Predictors of unplanned index hospitalization for top most expensive 5 conditions among senior HCUs

Covariates	AIM OR (95% CI)	P value	Fracture OR (95% CI)	P value	Cerebral infarction OR (95% CI)	P value	CHF OR (95% CI)	P value	COPD OR (95% CI)	P value
Age:										
75-84y **vs.** 66-74y	1.05 (0.99-1.12)	0.7996	2.3 (2.11-2.49)	<.0001	1.56 (1.44-1.7)	0.0006	1.78 (1.62-1.94)	0.6417	1.14 (1.06-1.24)	0.0032
>=85y vs. 66-74y	1.12 (1.03-1.22)	0.0188	4.06 (3.72-4.44)	<.0001	1.92 (1.75-2.12)	<.0001	3.05 (2.76-3.37)	<.0001	1.05 (0.95-1.17)	0.7335
Sex (M)	1.53 (1.45-1.63)	<.0001	0.46 (0.43-0.5)	<.0001	1.13 (1.05-1.21)	0.001	1.06 (0.99-1.14)	0.0919	1.11 (1.03-1.19)	0.0071
Low income status	1.07 (0.99-1.15)	0.1084	0.94 (0.87-1.02)	0.1232	1.09 (1-1.2)	0.0471	1.13 (1.04-1.23)	0.0056	0.98 (0.9-1.07)	0.6319
Rurality Index for Ontario, score	1 (1-1.01)	<.0001	1 (1-1)	0.0004	0.99 (0.99-0.99)	<.0001	1 (1-1)	0.0129	1 (1-1)	0.1301
Immigrant status	1.05 (0.88-1.25)	0.6063	0.96 (0.77-1.19)	0.7184	1.09 (0.89-1.33)	0.4023	0.92 (0.73-1.17)	0.5191	0.97 (0.74-1.28)	0.8338
Malignancy	0.68 (0.63-0.72)	<.0001	0.83 (0.77-0.89)	<.0001	0.68 (0.62-0.73)	<.0001	0.74 (0.68-0.8)	<.0001	0.76 (0.7-0.82)	<.0001
Hypertension	1.15 (1.08-1.22)	<.0001	1.03 (0.96-1.1)	0.4391	1.34 (1.24-1.44)	<.0001	1.19 (1.1-1.28)	<.0001	0.87 (0.81-0.94)	0.0002
Congestive heart failure (CHF)	1.16 (1.06-1.26)	0.0011	1.02 (0.93-1.12)	0.7105	1.29 (1.16-1.42)	<.0001	5.16 (4.78-5.56)	<.0001	1.48 (1.36-1.62)	<.0001
History of myocardial infarction	2.33 (2.13-2.55)	<.0001	1.18 (1.04-1.35)	0.0101	1.39 (1.23-1.58)	<.0001	1.45 (1.31-1.61)	<.0001	1.04 (0.92-1.18)	0.5676
Chronic Obstructive Pulmonary Disease (COPD)	1.03 (0.96-1.1)	0.4529	1.16 (1.08-1.24)	<.0001	1 (0.92-1.09)	0.9637	1.07 (0.99-1.16)	0.0762	14.03 (12.8-15.37)	<.0001
Diabetes	1 (0.94-1.07)	0.9908	0.79 (0.74-0.85)	<.0001	0.99 (0.91-1.07)	0.7299	1.26 (1.17-1.35)	<.0001	0.6 (0.55-0.65)	<.0001
Rheumatoid arthritis	1.04 (0.87-1.24)	0.6965	1.56 (1.33-1.83)	<.0001	1.01 (0.82-1.26)	0.8981	1.04 (0.85-1.28)	0.7109	1.04 (0.86-1.26)	0.6953
Mental health condition	0.86 (0.81-0.92)	<.0001	1.03 (0.96-1.1)	0.4202	0.92 (0.85-0.99)	0.0209	0.84 (0.78-0.9)	<.0001	0.95 (0.88-1.02)	0.1581
LTC residence	0.15 (0.06-0.38)	<.0001	0.4 (0.28-0.59)	<.0001	0.27 (0.13-0.56)	0.0004	0.29 (0.16-0.53)	<.0001	0.23 (0.11-0.48)	<.0001
Primary care enrollment										
Capitation vs. FFS	0.91 (0.82-1.01)	0.0526	0.84 (0.76-0.94)	0.0128	0.85 (0.75-0.96)	0.0005	0.81 (0.71-0.91)	0.0019	1.08 (0.94-1.24)	0.0606
Enhanced FFS vs. FFS	0.93 (0.83-1.03)	0.1639	0.82 (0.73-0.92)	0.002	0.84 (0.75-0.95)	0.0004	0.81 (0.71-0.91)	0.0028	1.06 (0.92-1.21)	0.0222
Family health team vs. FFS	0.89 (0.8-0.99)	0.0098	0.88 (0.78-0.98)	0.1244	0.85 (0.75-0.96)	0.0006	0.9 (0.8-1.02)	0.5013	1.08 (0.94-1.24)	0.0659
No provider identified vs. FFS	1.06 (0.89-1.27)	0.2201	1.14 (0.94-1.39)	0.0068	1.5 (1.23-1.83)	<.0001	1.46 (1.16-1.84)	<.0001	1.4 (1.09-1.81)	0.0687
Prescription drugs	0.97 (0.96-0.97)	<.0001	0.95 (0.94-0.96)	<.0001	0.94 (0.93-0.95)	<.0001	1.01 (1-1.01)	0.2352	1.05 (1.05-1.06)	<.0001
Emergency department visits	1.05 (1.02-1.08)	0.0008	1.02 (0.99-1.05)	0.2613	1.01 (0.97-1.05)	0.571	0.99 (0.95-1.02)	0.3894	1.07 (1.04-1.1)	<.0001
Visits to general practitioner	0.99 (0.98-0.99)	<.0001	1 (0.99-1.01)	0.8979	1 (0.99-1)	0.1243	1 (0.99-1)	0.7077	0.98 (0.97-0.98)	<.0001
Visits to specialist	0.92 (0.91-0.93)	<.0001	0.93 (0.92-0.93)	<.0001	0.93 (0.93-0.94)	<.0001	0.95 (0.95-0.96)	<.0001	0.94 (0.93-0.95)	<.0001
Visit to a geriatrician	0.60 (0.48-0.75)	<.0001	0.89 (0.76-1.05)	0.1561	0.75 (0.6-0.93)	0.0084	0.61 (0.49-0.75)	<.0001	0.63 (0.49-0.81)	0.0002
Homecare visits										
nursing	0.99 (0.98-1)	0.0035	0.99 (0.98-1)	0.0041	0.99 (0.98-1)	0.0096	0.99 (0.99-1)	0.0756	0.99 (0.99-1)	0.1523
personal support	0.99 (0.99-1)	<.0001	0.99 (0.99-1)	<.0001	1 (0.99-1)	<.0001	0.99 (0.99-1)	<.0001	1 (0.99-1)	<.0001
allied health	0.96 (0.92-1)	0.0522	0.99 (0.96-1.02)	0.6209	0.97 (0.93-1.02)	0.2188	1 (0.97-1.04)	0.9914	1 (0.96-1.04)	0.9425
social	0.82 (0.79-0.84)	<.0001	0.92 (0.91-0.94)	<.0001	0.85 (0.83-0.88)	<.0001	0.92 (0.9-0.94)	<.0001	0.91 (0.89-0.93)	<.0001
C-statistics	0.73		0.75		0.71		0.78		0.85	
C-statistics (cross-validated)	0.73		0.75		0.71		0.78		0.85	

AIM- Acute myocardial infarction, COPD- Chronic Obstructive Pulmonary Disease (COPD), CHF- Congestive heart failure (CHF), FFS- fee for service

Chapter 6
Conclusions

Although the phenomenon of a high-cost healthcare user has been known for decades, it is only relatively recently that researchers launched substantial efforts into exploring the issue in Canada (Wammes et al., 2018). Previous studies largely originated from the US (Wammes et al., 2018). Transferability of their results to the Canadian settings however is limited leaving gaps in our understanding of HCUs. At the same time, heterogeneity of the HCU population coupled with the lacking evidence of success of HCU targeting interventions have prompted policy makers and researchers to revise their management strategies and to seek specific segments of the HCU population who may benefit from certain interventions better than others(Figueroa, Joynt Maddox, et al., 2017; Karen E. Joynt et al., 2017; Tamang et al., 2017). Despite seniors constituting a large segment of the population(Rais et al., 2013; Wodchis et al., 2016), there is a lack of information on senior HCUs in Canada in general, whereas incident (or new) senior HCUs represent one distinct segment deemed worth investigating.

For the first time in Canada, we have examined new senior HCUs in the province of Ontario from a cross-sectional and longitudinal perspectives using advanced analytical approaches with innovative data presentation. This thesis advances the knowledge about HCUs in Canada in several ways. It describes various characteristics of particular segments of the population (e.g., seniors, incident HCUs, index hospitalizations) which is a unique contribution by itself, especially in the Canadian context. The thesis travels into unchartered waters by examining aspects that were not previously explored for this population (incremental costs, variation in access to care vs variation in costs, healthcare predictors of IHs). Finally, in addition to the comparison with matched senior non-HCUs, it applies advanced econometric methodologies (e.g. method of recycled predictions, two-part multi-level modelling of healthcare expenditures) borrowed from the field of health economics which also highlights the collaborative nature of the thesis.

The text below summarises the findings of this thesis for each of the three inter-related research questions. We also discuss policy and research implications, and comment on other methodological approaches that can be applied in the future to further our understanding of this population.

Research question 1: What is the one-year incremental healthcare utilization and direct financial impact on public payers of becoming an incident HCU among seniors in Ontario?

Almost every 10th senior in the province became a new HCU in 2013 by reaching the threshold of CAD $10,192 healthcare dollars spent. The provincial HCU rate was 94 HCUs per 1000 seniors. We determined that senior HCU incurred an additional mean of $25,527 per patient in total incremental public healthcare expenditures. Our dataset contained all senior HCUs in the province for 2013, therefore the estimated total financial impact can reasonably be stated as one tenth of the entire provincial healthcare budget in the incident year (FY2013).

We determined that although senior HCUs were already on the upward trajectory during the year before the HCU status showing higher healthcare utilization and costs in the pre-incident year, the HCU status was associated with a spike in healthcare expenditures. This rejects a potential hypothesis that HCUs might have been already approaching the threshold in the pre-incident year and it would merely take them a few extra healthcare services to become an HCU.

We found that although seniors became HCU through incurring costs in various combinations, half of the senior HCUs reached HCU status by incurring costs from only one or two categories, dominated by prolonged hospital admission. Approximately 12% of senior HCUs had no hospitalization expenditures in the incident year. These seniors achieved the HCU status through incurring predominantly physician, medication, and laboratory costs.

Overall, hospitalizations, physician compensation, then medications reimbursed by ODB were responsible for the highest incremental costs. In addition, this thesis revealed that several categories were associated almost exclusively with the incident senior HCU status: costs of rehabilitation, complex continuing care, dialysis and mental health admission were close to zero during the pre-incident year followed by an escalation of healthcare expenditures in the incident year among HCUs. Separately from the costs, examination of care utilization categories showed that urgent admissions accounted for the largest proportion of hospitalizations, whereas specialist visits and personal support visits were responsible for the greatest number of physician encounters and nursing visits, respectively.

In summary, by comparing HCUs with a matched cohort of non-HCUs, the main contributions of this chapter are three-fold: 1) clarification of the role of 12 healthcare categories in the senior HCU conversion; 2) identification of a subgroup of the population that became HCU without hospital admission and therefore is worth further investigation because prevention of HCU status among them may be different than in the rest of HCUs; and 3) estimation of the fiscal impact of the senior HCUs on the provincial budget using economics methods.

Research question 2: What is the extent of regional (health planning level) variation in healthcare costs and mortality among senior incident HCUs compared to non-HCUs in Ontario?

The senior HCU rate varied across the province ranging from 88.1 to 100.2 per 1000 seniors per LHIN. We found that overall regional variation in total costs was low in both cohorts. However, judging by adjusted variance estimates (both part 1 and part 2 of the model) of individual cost components, the variability was greater in accessing the healthcare system - once the patient entered the system, variation in costs was low. LHIN-specific variation in dialysis costs had the highest significant values in HCUs, whereas regional variation in cancer expenditures was an outlier among non-HCUs. Further, much of the observed variation in the probability of accessing healthcare was explained by the covariates traditionally representing health care needs (e.g., age, sex, health status). Once the costs were incurred however, the role of these covariates in explaining observed variation greatly diminished. Importantly, these traditional covariates explain much less variation for HCUs on average compared with non-HCUs.

Our findings indicate that reporting variation in total spending alone hides the contribution of individual cost components. The magnitude of some cost components such as hospitalization (a mean of $13,677 among HCU) absorbs the variation of smaller components (a mean of $181 in lab costs, for instance). As shown by the results of this chapter, examining regional variation as a function of total costs only would present an incomplete picture: e.g., although small regional variation in total costs, there is a much greater variation in dialysis costs among HCU.

We determined that all-cause mortality during the incident year among HCUs (104.2 per 1000) was 13.6 times greater that of non-HCU (7.7 per 1000). Observed LHIN-specific variation in mortality was however 10 times as low among HCUs. This suggests that there was a 10.4% risk of dying once a senior becomes an HCU regardless of the place of residence within the province.

We have also studied the relationship between the total costs and mortality for HCU and non-HCU across Ontario LHINs to explore health system performance from the efficiency angle. Building on the approach used in hospital profiling (D'Errigo, Tosti, Fusco, Perucci, & Seccareccia, 2007; MacKenzie et al., 2015; M. Zhang, Strawderman, Cowen, & Wells, 2006), we modified data presentation and plotted random effects for LHINs against the random effects for mortality in a cost-mortality plane where the X-axis represents the distribution of REs for mortality and the Y-axis is REs for costs, intersecting at 0. As such, our results provide insight into the distribution of mortality in relation to resources spent across the LHINs by identifying districts of various cost-mortality performance: LHINs in the upper right quadrant (high cost and high mortality) can be considered as those of lower efficiency where LHINs in the lower left quadrant are of higher efficiency (low costs and low mortality). Although the observed differences in efficiency between health regions merit further examination to determine if health improvement could be achieved without additional healthcare spending, caution should be applied when interpreting the efficiency results for two reasons. First, variation in total costs across LHINs appears quite small in magnitude, despite its statistical significance. Second, all-cause mortality was used in the calculations. Compared to preventable mortality, all-cause mortality is affected by a variety of factors, not all of which are amenable to health care amelioration.

In summary, the main contributions of this chapter are 1) confirmed equal risk-adjusted allocation of resources across LHINs among seniors overall, although some inequalities exist among individual cost categories, especially dialysis and cancer care; 2) identified considerable variation in access to various types of care; 3) ascertained lower variation in mortality among HCUs compared with senior non-HCUs, 4) determined a minor role for traditional cost and variation drivers in HCUs; and 5) explored a cost-mortality relationship by health districts suggesting a need for further investigation.

Research question 3: What are the characteristics of hospital admissions and associated costs in senior incident HCUs compared to non-HCUs in Ontario?

By examining the first hospitalization among incident cases of senior HCUs we found that unplanned IHs were considerably more common among HCUs: 70% of all senior HCUs compared to 2% of non-HCUs. Ten conditions, many of which have known remediable risk factors for hospitalization (An et al., 2017; Del Gobbo et al., 2015; Lim & Kwon, 2010; Woolf & Åkesson, 2003; Yusuf et al., 2004), accounted for a large number of HCU admissions and one third of their hospitalization costs. Besides a higher admission rate, HCUs had longer hospital stays and were more frequently designated as alternate level of care (ALC). Although lower in costs compared with acute care patients (Sutherland JM & Crump, 2011), the additional ALC days also contribute to HCU conversion (Ronksley et al., 2016). Longer hospital stays and longer ALC stays are the hallmark of senior HCU unplanned IHs.

We noticed a striking difference in inpatient mortality between the cohorts: non-HCU patients were more than twice as likely to die in hospital compared to HCUs (14.0% vs. 6.4%, standardised difference: 0.25), despite the HCUs' longer mean acute length of stay. Among those who died in hospital, non-HCUs also had a substantially shorter stay before death (2.3 vs. 17.9 days, standardised difference: 0.87). Given the 10.4% overall mortality among senior HCUs in the incident year, this observation suggests that many of them are chronically ill who were stabilized during admission and died outside the hospital (in the community or other institutions) following discharge. The relatively high inpatient mortality rate among non-HCUs constitutes approximately 30% of non-HCU deaths in the incident year. This supports the evidence that a large proportion of seniors still spend their last days of life in hospitals (Jayaraman & Joseph, 2013; Motiwala, Croxford, Guerriere, & Coyte, 2006), although there is a decreasing trend in favor of alternative institutions (Teno, Gozalo, Bynum, & et al., 2013).

Our findings point to many similarities in the predictors of the first unplanned admission between the two cohorts such as age, male sex or various chronic conditions which is in line with previous predictive studies of hospitalization among seniors in general (Wallace et al., 2014). Although the magnitude of many predictors was low (i.e., OR is very close to 1), including the number of medications dispensed, the effects of family practitioner visits, or home care services, a few predictors unique to each cohort showed noticeable protective association with the risk of admission. The analyses suggest that increasing access to geriatricians and other specialists is associated with reduced IHs among seniors. Factors such as attachment to a primary care provider or living in a long-term care facility may be associated with lower risk for IHs among HCUs. In contrast to the predictors with a low magnitude of association, the "other" category of home care services (a combination of social services, respite care and case management) had some protective effect in IHs among HCUs. Also, our findings suggest that recent senior immigrants were less likely to become HCUs or be admitted with an IH, supporting earlier reports of the "healthy immigrant" effect (Vang et al., 2017). This chapter has also looked at the baseline predictors of in-patient mortality in both cohorts. Analogous to the predictors of IHs, most predictors of inpatient mortality were similar in the two cohorts. Visiting an ED, seeing a specialist, and primary care provider attachment were associated with lower mortality in both cohorts.

In summary, the main contributions of this chapter are 1) corroborated findings of chapter 3 (Research Question 1) and confirmed the major role of prolonged hospital admissions in senior HCU conversion by focusing on the unplanned first hospitalization during the incident year; 2) explored unplanned IH predictors extending into the healthcare provided prior to the conversion and identified potential targets for policy interventions.

Policy and research implications

The findings of this doctoral thesis have multiple implications for health policy and future research. The text below will present a combination of both.

As a sign of reassurance for health administrators, the thesis demonstrates that allocation of resources to the senior population across the provincial health districts is equal: there is little variation in total healthcare expenditures, once the costs are incurred. Some may even argue that vertical equity is in place too: seniors with a higher disease burden receive more care. However, it is the access to care not healthcare expenditures that should become the priority for future investigation, especially in care categories that were outliers in variation (i.e., dialysis and cancer care). First, attempts should be made to explore other factors that explain variation in access to healthcare services beyond the traditional drivers. Second, it is unknown whether variation in access and costs was present in the pre-incident year and what was the impact of that on HCU conversion during the incident year.

The thesis' findings point toward a few factors that have either a protective effect of the first admission in the incident year for HCUs or affect the total length of stay once the patient is admitted, hence have the potential to reduce the role of IHs in HCU conversion among seniors. Specifically, we described the role of healthcare predictors of IHs (e.g., outpatient visits, dispensed medications, etc.). Further investigation is however required into some of them. First, a closer look into the "other" category of home care services would help tease out its components (i.e., social services, respite care or case management) that have the most protective effect on IHs among HCUs. Second, examining variation in access to geriatric outpatient care would help better understand whether improved access is associated with lower odds of IHs. Also, linking physician attributes (gender, years in practice, number of patients cared for, location of practice, referral privileges, etc.) with HCU outcomes would allow decision makers to identify geriatricians most suitable for targeted interventions. Similarly, although LTC costs contribute to HCU conversion, placement with a LTC facility, when needed, reduces the risk of IHs and may subsequently curb the conversion. Therefore, examining access to LTC beds and modeling its effect on IHs can add clarity. Also, further understanding is required on whether LTC admissions are specifically related to reductions in the use of acute care (in contrast to other discharge destinations. Third, and more importantly, we studied the quantity or intensity of past health care use, i.e., the frequency of visits or the number of outpatient drugs, but yet to describe the nature and quality of the visits and prescription practices that may be associated with the HCU conversion.

The role of primary care provider attachment on IHs can also be clarified by future research. This thesis shows the protective effect of such attachment in reference to orphan HCU patients. However, more in-depth analysis can elucidate the role of various types of primary care models in reference to each other. Reforms in the past two decades in Ontario have reduced the prevalence of practices with FFS from 80% in 2003 to 28% by 2013 (Sweetman A & Buckley G, 2014). Evidence shows however that the reforms may not have been able to reduce the use of care, for examples, ED visits (Glazier RH, 2012.). What effect various models have on HCU conversion is also unclear. This is in line with a general lack of research evaluating the primary care reforms in Ontario (Marchildon & Hutchison, 2016).

Further, the cost reduction rhetoric has dominated HCU research. However, it remains unclear whether cost reduction is possible. Let's consider, for example, IHs and reduction of their costs. In the context of a public health care system of Ontario, there is a single payer in the province where the majority of the hospitals are funded through global budgets. When patients have a reduced admission rate, hospitals continue admitting other patients waiting in the emergency rooms or those in queue for an elective procedure. Therefore, from the perspective of the single payer, the intervention may not necessarily lead to reduced healthcare expenditures. In fact, if the intervention is associated with increased outpatient care to keep these patients from the hospitals, the costs to the system as a whole may increase. Similarly, the expected effect of reduction in the proportion of ALC patients on hospitalization costs may not be possible without changing hospital funding (e.g., Ontario funding reform(Palmer et al., 2018)) and improving post-discharge options (e.g., "Home First", long-term care)(Lavergne RM, 2015; Sutherland JM & Crump, 2011). But the latter again requires additional funding. The indirect benefits of such an approach however are more patients that in need for care receive it either at the ambulatory or inpatient level provided that care is appropriate. An economic evaluation from a health system perspective that employs microsimulation modeling and a budget impact analysis would likely provide more definitive answers. Eventually, better cost re-allocation instead of cost reduction can become the new rhetoric with respect to HCUs.

The impact that immigration to Canada has on all sectors of the society are of great importance to policy makers. The support that our analysis provided for the healthy immigrant effect by identifying a lower HCU rate and a reduced risk of IHs among recent senior immigrants has reassured the Canadian Immigration, Refugee and Citizenship Agency (CIRC) (in personal communication) in the effectiveness of the excessive demand assessment policy. This policy prevents those immigrants from entering Canada who may potentially strain the Canadian health care system if admitted due to high care demands. Since some immigrant categories (e.g., refugees) are exempt from the policy, investigating their contribution toward the senior HCUs can inform future CIRC actions.

Finally, in addition to the methodological contributions of this doctoral thesis (e.g. the first attempt to describe a sub-population of HCUs, comparison with a matched group, use of random effects models to examine regional variation in outcomes, use of recycled predictions to determine the incremental costs and healthcare utilization associated with the HCU status, focus on index hospitalizations during the incident year), there are several future methodological considerations. First, future cost analysis of senior HCUs could benefit from higher data granularity and more longitudinal patient care-centered approaches (Guilcher et al., 2016). Following a patient by type of care received in the incident year, for example, one may clarify the point of HCU conversion, differentiate between outpatient and inpatient costs that contribute to it, and allocate costs more accurately (e.g., physician costs as part of hospital expenditures). In the spirit of continuing inter-sectoral collaboration, the method of multi-touch attribution can be used to not only identify the chronology that leads to the HCU conversion but also better describe the interactions between various types of care along the way (Shao X & L, 2011). Once the chronology is established, HCU conversion can be simulated using methods such as discrete event simulation to evaluate effectiveness and cost-effectiveness of HCU prevention interventions (X. Zhang, 2018).

Second, the estimates of geographical variation in health outcomes can be further adjusted by accounting for possible inter-unit dependence (i.e., spatial correlation) (Chaix, Merlo, & Chauvin, 2005; Dong, Harris, Jones, & Yu, 2015; Ouédraogo et al., 2018; Schootman, Chien, Yun, & Pruitt, 2016). Bayesian-based simulation approaches (e.g., hierarchical spatial autoregressive modelling) can be applied to assess the interaction between subjects from neighboring geographical units (spatial interactions) and the influence of unit-dependent contextual factors (spatial proximity effects) on the outcome, (Dong et al., 2015; Ouédraogo et al., 2018). Third, further clustering of HCUs patients can be performed using statistically sound approaches such as the latent variable analysis (Yan, Kwan, Tan, Thumboo, & Low, 2018). Now that we have explored the association of individual predictors of IHs, for example, we can shift our efforts toward determining combinations of these predictors and the corresponding patient clusters that these combinations may form within each cohort to advance our knowledge of admitted HCUs.

In summary, by answering three research questions, this thesis has advanced our knowledge of the HCU population in Canada by focusing on the segment of new senior HCUs in comparison to matched senior non-HCUs and using advanced statistical analysis; identified areas that are relevant for health policy makers with respect to the management of the group; and proposed avenues for further investigation.

References

AHRQ Quality Indicators—Prevention Quality Indicators Technical Specifications Updates. (July 2016). Version 6.0 (ICD 10). Retrieved from http://www.qualityindicators.ahrq.gov/Modules/PQI_TechSpec_ICD10_v60.aspx

An, S. J., Kim, T. J., & Yoon, B. W. (2017). Epidemiology, Risk Factors, and Clinical Features of Intracerebral Hemorrhage: An Update. *J Stroke, 19*(1), 3-10. doi:10.5853/jos.2016.00864

Austin, P. C., van Walraven, C., Wodchis, W. P., Newman, A., & Anderson, G. M. (2011). Using the Johns Hopkins Aggregated Diagnosis Groups (ADGs) to predict mortality in a general adult population cohort in Ontario, Canada. *Med Care, 49*(10), 932-939. doi:10.1097/MLR.0b013e318215d5e2

Basu, A., Arondekar, B. V., & Rathouz, P. J. (2006). Scale of interest versus scale of estimation: comparing alternative estimators for the incremental costs of a comorbidity. *Health Econ, 15*(10), 1091-1107. doi:10.1002/hec.1099

Basu, A., Manning, W. G., & Mullahy, J. (2004). Comparing alternative models: log vs Cox proportional hazard? *Health Econ, 13*(8), 749-765. doi:10.1002/hec.852

Bleich, S. N., Sherrod, C., Chiang, A., Boyd, C., Wolff, J., DuGoff, E., . . . Anderson, G. (2015). Systematic Review of Programs Treating High-Need and High-Cost People With Multiple Chronic Diseases or Disabilities in the United States, 2008–2014. *Preventing Chronic Disease, 12*, E197. doi:10.5888/pcd12.150275

Blumenthal, D., Chernof, B., Fulmer, T., Lumpkin, J., & Selberg, J. (2016). Caring for High-Need, High-Cost Patients - An Urgent Priority. *N Engl J Med, 375*(10), 909-911. doi:10.1056/NEJMp1608511

Canadian Institute for Health Information. (2017). *National Health Expenditure Trends, 1975 to 2017*. Retrieved from Ottawa, ON: https://www.cihi.ca/en/national-health-expenditure-trends

Canadian Institute for Health Information: Ambulatory Care Sensitive Conditions. (2016). Retrieved from http://indicatorlibrary.cihi.ca/display/HSPIL/Ambulatory+Care+Sensitive+Conditions

Central Midlands NHS. (2014). *The Total Cost of Care for Older People in Solihull - an Analysis of Combined NHS and Social Care Data*. Retrieved from https://solihullccg.nhs.uk/publications/1245-bcf-cost-of-care/file

Chaix, B., Merlo, J., & Chauvin, P. (2005). Comparison of a spatial approach with the multilevel approach for investigating place effects on health: the example of healthcare utilisation in France. *J Epidemiol Community Health, 59*(6), 517-526. doi:10.1136/jech.2004.025478

Chang, C., Lee, S. M., Choi, B. W., Song, J. H., Song, H., Jung, S., . . . Suh, D. C. (2017). Costs Attributable to Overweight and Obesity in Working Asthma Patients in the United States. *Yonsei Med J, 58*(1), 187-194. doi:10.3349/ymj.2017.58.1.187

Clough, J. D., Riley, G. F., Cohen, M., Hanley, S. M., Sanghavi, D., DeWalt, D. A., . . . Conway, P. H. (2016). Patterns of care for clinically distinct segments of high cost Medicare beneficiaries. *Healthc (Amst), 4*(3), 160-165. doi:10.1016/j.hjdsi.2015.09.005

D'Errigo, P., Tosti, M. E., Fusco, D., Perucci, C. A., & Seccareccia, F. (2007). Use of hierarchical models to evaluate performance of cardiac surgery centres in the Italian CABG outcome study. *BMC Med Res Methodol, 7*, 29. doi:10.1186/1471-2288-7-29

Dattalo, M., Nothelle, S., & Chapman, E. N. (2016). Targeting Enhanced Services Toward High-Cost, High-Need Medicare Patients *New Directions in Geriatric Medicine Concepts, Trends, and Evidence-Based Practice* (pp. 13-30).

de Oliveira, C., Bremner, K. E., Pataky, R., Gunraj, N., Chan, K., Peacock, S., & Krahn, M. D. (2013). Understanding the costs of cancer care before and after diagnosis for the 21 most common cancers in Ontario: a population-based descriptive study. *CMAJ Open, 1*(1), E1-E8. doi:10.9778/cmajo.20120013

de Oliveira, C., Cheng, J., Vigod, S., Rehm, J., & Kurdyak, P. (2016). Patients With High Mental Health Costs Incur Over 30 Percent More Costs Than Other High-Cost Patients. *Health Aff (Millwood), 35*(1), 36-43. doi:10.1377/hlthaff.2015.0278

Del Gobbo, L. C., Kalantarian, S., Imamura, F., Lemaitre, R., Siscovick, D. S., Psaty, B. M., & Mozaffarian, D. (2015). Contribution of Major Lifestyle Risk Factors for Incident Heart Failure in Older Adults: The Cardiovascular Health Study. *Jacc. Heart Failure, 3*(7), 520-528. doi:10.1016/j.jchf.2015.02.009

Densen, P. M., Shapiro, S., & Einhorn, M. (1959). Concerning High and Low Utilizers of Service in a Medical Care Plan, and the Persistence of Utilization Levels over a Three Year Period. *The Milbank Memorial Fund Quarterly, 37*(3), 217-250. doi:10.2307/3348768

Dimick, J. B., & Ryan, A. M. (2014). Methods for evaluating changes in health care policy: the difference-in-differences approach. *JAMA, 312*(22), 2401-2402. doi:10.1001/jama.2014.16153

Dong, G., Harris, R., Jones, K., & Yu, J. (2015). Multilevel Modelling with Spatial Interaction Effects with Application to an Emerging Land Market in Beijing, China. *PLoS One, 10*(6), e0130761. doi:10.1371/journal.pone.0130761

Elhai, J. D., Calhoun, P. S., & Ford, J. D. (2008). Statistical procedures for analyzing mental health services data. *Psychiatry Res, 160*(2), 129-136. doi:10.1016/j.psychres.2007.07.003
Expenditure Estimates for the Ministry of Health and Long Term Care (2018-19). Retrieved from https://www.ontario.ca/page/expenditure-estimates-ministry-health-and-long-term-care-2018-19
Figueroa, J. F., Frakt, A. B., Lyon, Z. M., Zhou, X., & Jha, A. K. (2017). Characteristics and spending patterns of high cost, non-elderly adults in Massachusetts. *Healthc (Amst), 5*(4), 165-170. doi:10.1016/j.hjdsi.2017.05.001
Figueroa, J. F., Joynt Maddox, K. E., Beaulieu, N., Wild, R. C., & Jha, A. K. (2017). Concentration of Potentially Preventable Spending Among High-Cost Medicare Subpopulations: An Observational Study. *Ann Intern Med, 167*(10), 706-713. doi:10.7326/m17-0767
Fitzpatrick, T., Rosella, L. C., Calzavara, A., Petch, J., Pinto, A. D., Manson, H., . . . Wodchis, W. P. (2015). Looking Beyond Income and Education: Socioeconomic Status Gradients Among Future High-Cost Users of Health Care. *Am J Prev Med, 49*(2), 161-171. doi:10.1016/j.amepre.2015.02.018
Ganguli, I., Thompson, R. W., & Ferris, T. G. (2017). What can five high cost patients teach us about healthcare spending? *Healthc (Amst), 5*(4), 204-213. doi:10.1016/j.hjdsi.2016.12.004
Gershon, A. S., Wang, C., Guan, J., Vasilevska-Ristovska, J., Cicutto, L., & To, T. (2009). Identifying individuals with physcian diagnosed COPD in health administrative databases. *Copd, 6*(5), 388-394.
Glazier RH, Z. B., Rayner J. (2012.). *Comparison of Primary Care Models in Ontario by Demographics, Case Mix and Emergency Department Use, 2008/09 to 2009/10*. Retrieved from Toronto:
Graverholt, B., Riise, T., Jamtvedt, G., Ranhoff, A. H., Kruger, K., & Nortvedt, M. W. (2011). Acute hospital admissions among nursing home residents: a population-based observational study. *BMC Health Serv Res, 11*, 126. doi:10.1186/1472-6963-11-126
Gregori, D., Petrinco, M., Bo, S., Desideri, A., Merletti, F., & Pagano, E. (2011). Regression models for analyzing costs and their determinants in health care: an introductory review. *Int J Qual Health Care, 23*(3), 331-341. doi:10.1093/intqhc/mzr010
Guilcher, S. J., Bronskill, S. E., Guan, J., & Wodchis, W. P. (2016). Who Are the High-Cost Users? A Method for Person-Centred Attribution of Health Care Spending. *PLoS One, 11*(3), e0149179. doi:10.1371/journal.pone.0149179
Hay, C., Pacey, M., Bains, N., & Ardal, S. (2010). Understanding the Unattached Population in Ontario: Evidence from the Primary Care Access Survey (PCAS). *Healthc Policy, 6*(2), 33-47.
Hensel, J. M., Taylor, V. H., Fung, K., & Vigod, S. N. (2016). Rates of Mental Illness and Addiction among High-Cost Users of Medical Services in Ontario. *Can J Psychiatry, 61*(6), 358-366. doi:10.1177/0706743716644764
Holtz-Eakin, D. (2005). High-Cost Medicare Beneficiaries Retrieved from http://www.cbo.gov/publication/16487
Hosmer DW, & Lemeshow S. (2000). *Applied Logistic Regression (2nd Edition)*. New York, NY: John Wiley & Sons.

Institute for Competitiveness & Prosperity. (2014). Building Better Health Care: Policy opportunities for Ontario. *Working Paper 20.* Retrieved from https://www.competeprosper.ca/uploads/WP20_BetterHealthCare_FINAL.pdf
Jayaraman, J., & Joseph, K. (2013). Determinants of place of death: a population-based retrospective cohort study. *BMC Palliat Care, 12*, 19. doi:10.1186/1472-684x-12-19
Johns Hopkins ACG® System Version 10.0. (2014). Technical Reference Guide.
Joynt, K. E., Figueroa, J. F., Beaulieu, N., Wild, R. C., Orav, E. J., & Jha, A. K. (2017). Segmenting high-cost Medicare patients into potentially actionable cohorts. *Healthcare, 5*(1), 62-67. doi:https://doi.org/10.1016/j.hjdsi.2016.11.002
Joynt, K. E., Gawande, A. A., Orav, E. J., & Jha, A. K. (2013). Contribution of preventable acute care spending to total spending for high-cost Medicare patients. *JAMA, 309*(24), 2572-2578. doi:10.1001/jama.2013.7103
Kralj B. (2000). Measuring 'rurality' for purposes of health-care planning: an empirical measure for Ontario. *Ontario Medical Review, October*, 33-52.
Kramer, A. A., & Zimmerman, J. E. (2007). Assessing the calibration of mortality benchmarks in critical care: The Hosmer-Lemeshow test revisited. *Crit Care Med, 35*(9), 2052-2056. doi:10.1097/01.ccm.0000275267.64078.b0
Ku, L. J., Chiou, M. J., & Liu, L. F. (2015). Variations in the persistence of health expenditures and the implications for the design of capitation payments in Taiwan. *J Health Serv Res Policy, 20*(3), 146-153. doi:10.1177/1355819615577711
Lange, A., Zeidler, J., & Braun, S. (2014). One-year disease-related health care costs of incident vertebral fractures in osteoporotic patients. *Osteoporos Int, 25*(10), 2435-2443. doi:10.1007/s00198-014-2776-4
Lavergne RM. (2015). *Regional variation in Alternate Level of Care (ALC) service use in British Columbia hospitals: An opportunity for intervention?* Retrieved from Institute for Health System Transformation & Sustainability; :
Lee, J. Y., Muratov, S., Tarride, J. E., & Holbrook, A. M. (2018). Managing High-Cost Healthcare Users: The International Search for Effective Evidence-Supported Strategies. *J Am Geriatr Soc*. doi:10.1111/jgs.15257
Lee, N. S., Whitman, N., Vakharia, N., Ph, D. G., & Rothberg, M. B. (2017). High-Cost Patients: Hot-Spotters Don't Explain the Half of It. *J Gen Intern Med, 32*(1), 28-34. doi:10.1007/s11606-016-3790-3
Lieberman, S. M., Lee, J., Anderson, T., & Crippen, D. L. (2003). Reducing the growth of Medicare spending: geographic versus patient-based strategies. *Health Aff (Millwood), Suppl Web Exclusives*, W3-603-613.
Lim, J.-S., & Kwon, H.-M. (2010). Risk of "silent stroke" in patients older than 60 years: risk assessment and clinical perspectives. *Clinical Interventions in Aging, 5*, 239-251.
Lui WS, & Cela J. (2008). Count Data Models in SAS. Retrieved from http://www2.sas.com/proceedings/forum2008/371-2008.pdf
Lungu E., & Warwick G. Potential Savings from Biosimilars in Canada. *Presentation in 2017 CADTH Symposium.* Retrieved from https://www.cadth.ca/sites/default/files/symp-2017/presentations/april24-2017/Concurrent-Session-B4-Gary-Warwick.pdf
MacKenzie, T. A., Grunkemeier, G. L., Grunwald, G. K., O'Malley, A. J., Bohn, C., Wu, Y., & Malenka, D. J. (2015). A primer on using shrinkage to compare in-hospital mortality

between centers. *Ann Thorac Surg, 99*(3), 757-761. doi:10.1016/j.athoracsur.2014.11.039

Mamdani, M., Sykora, K., Li, P., Normand, S.-L. T., Streiner, D. L., Austin, P. C., . . . Anderson, G. M. (2005). Reader's guide to critical appraisal of cohort studies: 2. Assessing potential for confounding. *BMJ : British Medical Journal, 330*(7497), 960-962.

Mandrekar JN, & SJ, M. (2004). *An introduction to matching and its application using SAS (Proceedings of the Twenty-ninth Annual SAS Users Group International Conference, 29, 208 'Statistics and Data Analysis')*.

Manning, W. G., & Mullahy, J. (2001). Estimating log models: to transform or not to transform? *J Health Econ, 20*(4), 461-494.

Mannino, D. M., Higuchi, K., Yu, T. C., Zhou, H., Li, Y., Tian, H., & Suh, K. (2015). Economic Burden of COPD in the Presence of Comorbidities. *Chest, 148*(1), 138-150. doi:10.1378/chest.14-2434

Marchildon, G. P., & Hutchison, B. (2016). Primary care in Ontario, Canada: New proposals after 15 years of reform. *Health Policy, 120*(7), 732-738. doi:https://doi.org/10.1016/j.healthpol.2016.04.010

Mihaylova, B., Briggs, A., O'Hagan, A., & Thompson, S. G. (2011). Review of statistical methods for analysing healthcare resources and costs. *Health Econ, 20*(8), 897-916. doi:10.1002/hec.1653

Mondor, L., Walker, K., Bai, Y. Q., & Wodchis, W. P. (2017). Use of hospital-related health care among Health Links enrollees in the Central Ontario health region: a propensity-matched difference-in-differences study. *CMAJ Open, 5*(4), E753-E759. doi:10.9778/cmajo.20170054

Morgan S, & Persaud N. Generic drug prices could drop – if rebates are replaced with public tendering. Retrieved from https://healthydebate.ca/opinions/generic-drug-prices

Morgan, S. G., & Persaud, N. (2018). New generic pricing scheme maintains high prices and risks of shortages. *CMAJ, 190*(14), E410-e411. doi:10.1503/cmaj.180197

Motiwala, S. S., Croxford, R., Guerriere, D. N., & Coyte, P. C. (2006). Predictors of place of death for seniors in Ontario: a population-based cohort analysis. *Can J Aging, 25*(4), 363-371.

Muratov S, Lee J, Holbrook A, Paterson JM, Guertin JR, Mbuagbaw L, . . . TarrideJE. (2018). Regional Variation in Healthcare Spending and Mortality among Senior High-Cost Healthcare Users in Ontario, Canada: a retrospective matched cohort study. *BMC Geriatr*.

Muratov, S., Lee, J., Holbrook, A., Costa, A., Paterson, J. M., Guertin, J. R., . . . Tarride, J. E. (2018). Regional variation in healthcare spending and mortality among senior high-cost healthcare users in Ontario, Canada: a retrospective matched cohort study. *BMC Geriatr, 18*(1), 262. doi:10.1186/s12877-018-0952-7

Muratov, S., Lee, J., Holbrook, A., Paterson, J. M., Guertin, J. R., Mbuagbaw, L., . . . Tarride, J. E. (2017). Senior high-cost healthcare users' resource utilization and outcomes: a protocol of a retrospective matched cohort study in Canada. *BMJ Open, 7*(12), e018488. doi:10.1136/bmjopen-2017-018488

Nelson, L. (2012). *Lessons from Medicare's Demonstration Projectson Disease Management and Care Coordination*. Retrieved from Washington, D.C.:

Oliver, T. R., Lee, P. R., & Lipton, H. L. (2004). A Political History of Medicare and Prescription Drug Coverage. *Milbank Q, 82*(2), 283-354. doi:10.1111/j.0887-378X.2004.00311.x

Ontario's LHINs. (2017). Ontario's Local Health Integration Networks. Retrieved from www.lhins.on.ca
Ontario Ministry of Health and Long-term Care. (2018). Understadning Ontario's Drug Programs. Retrieved from http://www.health.gov.on.ca/en/public/programs/drugs/
Ouédraogo, A. M., Crighton, E. J., Sawada, M., To, T., Brand, K., & Lavigne, E. (2018). Exploration of the spatial patterns and determinants of asthma prevalence and health services use in Ontario using a Bayesian approach. *PLoS One, 13*(12), e0208205. doi:10.1371/journal.pone.0208205
Palmer, K. S., Brown, A. D., Evans, J. M., Marani, H., Russell, K. K., Martin, D., & Ivers, N. M. (2018). Standardising costs or standardising care? Qualitative evaluation of the implementation and impact of a hospital funding reform in Ontario, Canada. *Health Research Policy and Systems, 16*(1), 74. doi:10.1186/s12961-018-0353-6
Peikes, D., Chen, A., Schore, J., & Brown, R. (2009). Effects of care coordination on hospitalization, quality of care, and health care expenditures among Medicare beneficiaries: 15 randomized trials. *JAMA, 301*(6), 603-618. doi:10.1001/jama.2009.126
Pocock, S. J., Wang, D., Pfeffer, M. A., Yusuf, S., McMurray, J. J., Swedberg, K. B., . . . Granger, C. B. (2006). Predictors of mortality and morbidity in patients with chronic heart failure. *Eur Heart J, 27*(1), 65-75. doi:10.1093/eurheartj/ehi555
Pritchard, D., Petrilla, A., Hallinan, S., Jr., D. H. T., Schabert, V. F., & Dubois, R. W. (2016). What Contributes Most to High Health Care Costs? Health Care Spending in High Resource Patients. *Journal of Managed Care & Specialty Pharmacy, 22*(2), 102-109. doi:10.18553/jmcp.2016.22.2.102
Rais, S., Nazerian, A., Ardal, S., Chechulin, Y., Bains, N., & Malikov, K. (2013). High-cost users of Ontario's healthcare services. *Healthc Policy, 9*(1), 44-51.
Reid, R., Evans, R., Barer, M., Sheps, S., Kerluke, K., McGrail, K., . . . Pagliccia, N. (2003). Conspicuous consumption: characterizing high users of physician services in one Canadian province. *J Health Serv Res Policy, 8*(4), 215-224. doi:10.1258/135581903322403281
Riley, G. F. (2007). Long-term trends in the concentration of Medicare spending. *Health Aff (Millwood), 26*(3), 808-816. doi:10.1377/hlthaff.26.3.808
ROC analysis using validation data and cross validation. SAS Support. © SAS Institute Inc. Retrieved from http://support.sas.com/kb/39/724.html
Roemer, M. I., & Myers, G. W. (1956). Multiple Admissions to Hospital. *Canadian Journal of Public Health / Revue Canadienne de Sante'e Publique, 47*(11), 469-481.
Ronald, L. A., McGregor, M. J., McGrail, K. M., Tate, R. B., & Broemling, A. M. (2008). Hospitalization rates of nursing home residents and community-dwelling seniors in British Columbia. *Can J Aging, 27*(1), 109-115. doi:10.3138/cja.27.1.109
Ronksley, P. E., Kobewka, D. M., McKay, J. A., Rothwell, D. M., Mulpuru, S., & Forster, A. J. (2016). Clinical characteristics and preventable acute care spending among a high cost inpatient population. *BMC Health Serv Res, 16*, 165. doi:10.1186/s12913-016-1418-2
Roos, N. P., Shapiro, E., & Tate, R. (1989). Does a small minority of elderly account for a majority of health care expenditures? A sixteen-year perspective. *Milbank Q, 67*(3-4), 347-369.
Rosella, L. C., Fitzpatrick, T., Wodchis, W. P., Calzavara, A., Manson, H., & Goel, V. (2014). High-cost health care users in Ontario, Canada: demographic, socio-economic, and health status characteristics. *BMC Health Serv Res, 14*, 532. doi:10.1186/s12913-014-0532-2

Schootman, M., Chien, L., Yun, S., & Pruitt, S. L. (2016). Explaining large mortality differences between adjacent counties: a cross-sectional study. *BMC Public Health, 16*, 681. doi:10.1186/s12889-016-3371-8

Schultz, S. E., Rothwell, D. M., Chen, Z., & Tu, K. (2013). Identifying cases of congestive heart failure from administrative data: a validation study using primary care patient records. *Chronic Dis Inj Can, 33*(3), 160-166.

Shao X, & L, L. (2011). *Data-driven Multi-touch Attribution Models*. Paper presented at the Proceedings of the 17th ACM SIGKDD International Conference on Knowledge Discovery and Data Mining, San Diego, CA, USA. http://delivery.acm.org/10.1145/2030000/2020453/p258-shao.pdf?ip=130.113.109.55&id=2020453&acc=ACTIVE%20SERVICE&key=FD0067F557510FFB%2ED816932E3DB0B89D%2E4D4702B0C3E38B35%2E4D4702B0C3E38B35&__acm__=1543530707_9b88c33e3d7b4ae8fc446032c3bde664

Sinha, S. K. (2011). Why the elderly could bankrupt Canada and how demographic imperatives will force the redesign of acute care service delivery. *Healthc Pap, 11*(1), 46-51; discussion 86-91.

Stanton MW, R. M. (2006). *High Concentration of US Health Expenditures*. Retrieved from https://meps.ahrq.gov/data_files/publications/ra19/ra19.pdf

Statistics Canada. (2016). Population by year, by province and territory. Retrieved from http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/demo02a-eng.htm

Stock JH, & Watson MW. (; 2011). *Introduction to Econometrics* (3rd ed.): Pearson.

Sutherland JM, & Crump, R. T. (2011). *Exploring alternative level of care (ALC) and the role of funding policies: an evolving evidence base for Canada* Retrieved from https://www.cfhi-fcass.ca

Sutherland, J. M., & Crump, R. T. (2013). Alternative level of care: Canada's hospital beds, the evidence and options. *Healthc Policy, 9*(1), 26-34.

Sweetman A, & Buckley G. (2014). *Ontario's Experiment with Primary Care Reform*. Retrieved from University of Calgary:

Tamang, S., Milstein, A., Sørensen, H. T., Pedersen, L., Mackey, L., Betterton, J.-R., . . . Shah, N. (2017). Predicting patient 'cost blooms' in Denmark: a longitudinal population-based study. *BMJ Open, 7*(1), e011580. doi:10.1136/bmjopen-2016-011580

Teno, J. M., Gozalo, P. L., Bynum, J. W., & et al. (2013). Change in end-of-life care for medicare beneficiaries: Site of death, place of care, and health care transitions in 2000, 2005, and 2009. *JAMA, 309*(5), 470-477. doi:10.1001/jama.2012.207624

The pan-Canadian Pharmaceutical Alliance. Council of the Federation. (2018). . Retrieved from http://www.canadaspremiers.ca/pan-canadian-pharmaceutical-alliance/

Vang, Z. M., Sigouin, J., Flenon, A., & Gagnon, A. (2017). Are immigrants healthier than native-born Canadians? A systematic review of the healthy immigrant effect in Canada. *Ethn Health, 22*(3), 209-241. doi:10.1080/13557858.2016.1246518

Wallace, E., Stuart, E., Vaughan, N., Bennett, K., Fahey, T., & Smith, S. M. (2014). Risk prediction models to predict emergency hospital admission in community-dwelling adults: a systematic review. *Med Care, 52*(8), 751-765. doi:10.1097/mlr.0000000000000171

Walter P. Wodchis, Bushmeneva K, Nikitovic M, & McKillop I. (2013). *Guidelines on Person-Level Costing Using Administrative Databases in Ontario*. Retrieved from

Wammes, J. J. G., van der Wees, P. J., Tanke, M. A. C., Westert, G. P., & Jeurissen, P. P. T. (2018). Systematic review of high-cost patients' characteristics and healthcare utilisation. *BMJ Open, 8*(9), e023113. doi:10.1136/bmjopen-2018-023113

Wodchis WP. *The Concentration of Health Care Spending: Little Ado (yet) About Much (money). Presented at the Canadian Association for Health Services and Policy Research (CASHPR) 2012 Conference. Available at: https://www.cahspr.ca/web/uploads/presentations/C6.1_Walter_P._Wodchis.pdf. Accessed October 1, 2015*. Available at: https://www.cahspr.ca/web/uploads/presentations/C6.1_Walter_P._Wodchis.pdf.

Wodchis WP, Bushmeneva K, Nikitovic M, & McKillop I. (2013). *Guidelines on Person-Level Costing Using Administrative Databases in Ontario*. Retrieved from

Wodchis, W. P., Austin, P. C., & Henry, D. A. (2016). A 3-year study of high-cost users of health care. *CMAJ, 188*(3), 182-188. doi:10.1503/cmaj.150064

Woolf, A. D., & Åkesson, K. (2003). Preventing fractures in elderly people. *BMJ : British Medical Journal, 327*(7406), 89-95.

World Health Organization. (2018). Global Health Expenditure Database, 2000-2015. . Retrieved from http://apps.who.int/nha/database/ViewData/Indicators/en

Yan, S., Kwan, Y. H., Tan, C. S., Thumboo, J., & Low, L. L. (2018). A systematic review of the clinical application of data-driven population segmentation analysis. *BMC Med Res Methodol, 18*(1), 121. doi:10.1186/s12874-018-0584-9

Yusuf, S., Hawken, S., Ounpuu, S., Dans, T., Avezum, A., Lanas, F., . . . Lisheng, L. (2004). Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet, 364*(9438), 937-952. doi:10.1016/s0140-6736(04)17018-9

Zhang, M., Strawderman, R. L., Cowen, M. E., & Wells, M. T. (2006). Bayesian Inference for a Two-Part Hierarchical Model. *Journal of the American Statistical Association, 101*(475), 934-945. doi:10.1198/016214505000001429

Zhang, X. (2018). Application of discrete event simulation in health care: a systematic review. *BMC Health Services Research, 18*(1), 687. doi:10.1186/s12913-018-3456-4

Zhang, Y., Donohue, J. M., Newhouse, J. P., & Lave, J. R. (2009). The Effects Of The Coverage Gap On Drug Spending: A Closer Look At Medicare Part D. *Health Aff (Millwood), 28*(2), w317-w325. doi:10.1377/hlthaff.28.2.w317