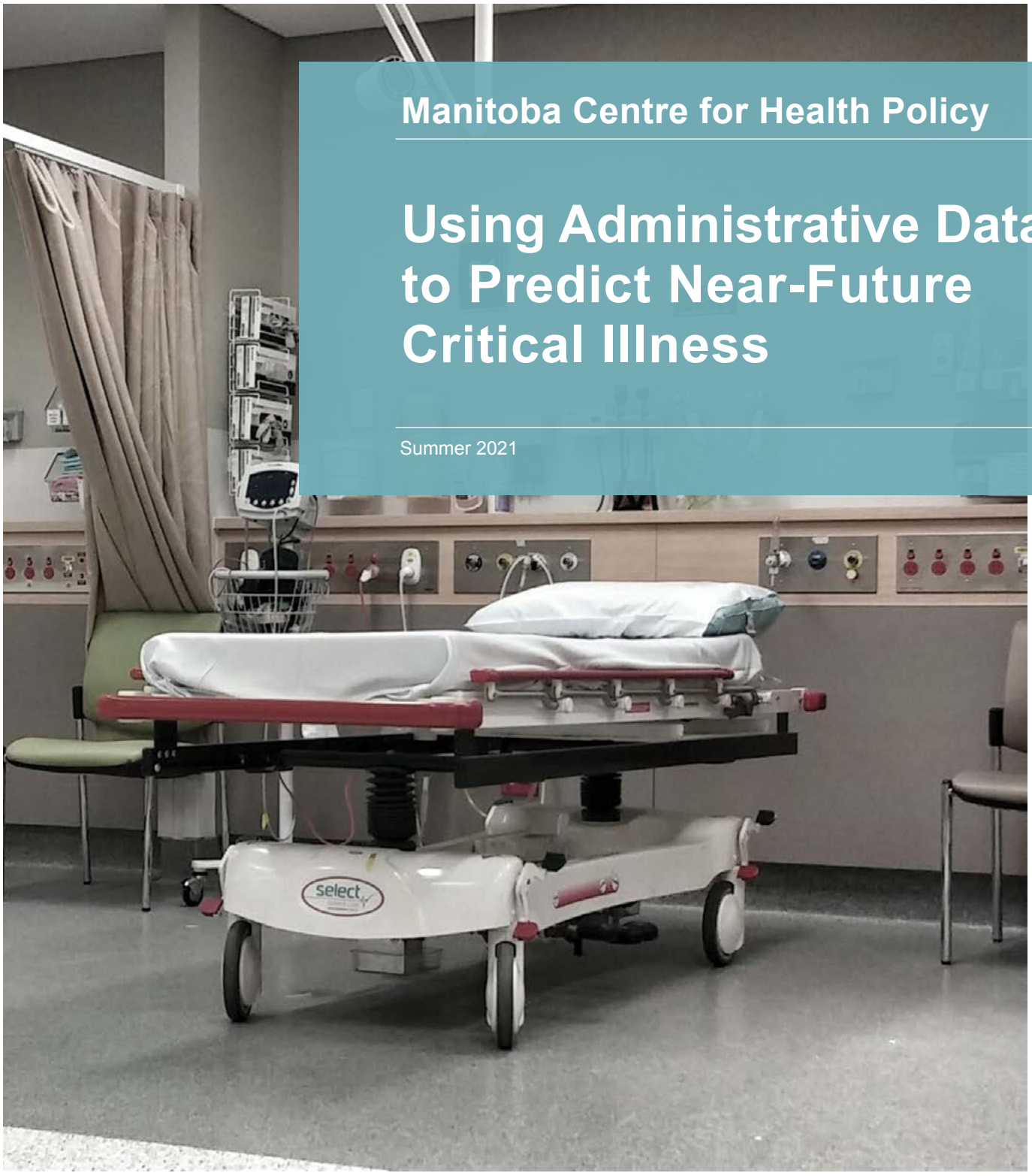

Manitoba Centre for Health Policy

Using Administrative Data to Predict Near-Future Critical Illness

Summer 2021

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Territory Acknowledgement

MCHP acknowledges that we live and work on Treaty 1 land, the home of the Anishinaabeg, Cree, Oji-Cree, Dakota and Dene peoples and the homeland of the Métis Nation. We respect the treaties that were made on these Territories, we acknowledge the harms and mistakes of the past, we recognize the ongoing present day colonial violence that is faced by Indigenous peoples within healthcare, education, justice, child welfare and government systems and we dedicate ourselves to moving forward in partnership towards decolonization in the spirit of reconciliation and collaboration.

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About the Manitoba Centre for Health Policy

The Manitoba Centre for Health Policy (MCHP) is located within the Department of Community Health Sciences, Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba. The mission of MCHP is to provide accurate and timely information to healthcare decision-makers, analysts and providers, so they can offer services which are effective and efficient in maintaining and improving the health of Manitobans. Our researchers rely upon the unique Manitoba Population Research Data Repository (Repository) to describe and explain patterns of care and profiles of illness and to explore other factors that influence health, including income, education, employment, and social status. This Repository is unique in terms of its comprehensiveness, degree of integration, and orientation around an anonymized population registry.

Members of MCHP consult extensively with government officials, healthcare administrators, and clinicians to develop a research agenda that is topical and relevant.

This strength, along with its rigorous academic standards, enables MCHP to contribute to the health policy process. MCHP undertakes several major research projects, such as this one, every year under contract to Manitoba Health and Seniors Care. In addition, our researchers secure external funding by competing for research grants. We are widely published and internationally recognized. Further, our researchers collaborate with a number of highly respected scientists from Canada, the United States, Europe, and Australia.

MCHP complies with all legislative acts and regulations governing the protection and use of sensitive information. We implement strict policies and procedures to protect the privacy and security of anonymized data used in our research and we keep the provincial Health Information Privacy Committee informed of all scientific work undertaken for Manitoba Health and Seniors Care.

The Manitoba Centre for Health Policy

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Abbreviations

ACG	Adjusted Clinical Group
ALC	Alternate level of care
CART	Classification and Regression Tree
CCI	Canadian Classification of Interventions
DAD	Discharge Abstract Database
DPIN	Drug Prescription Information Network
FY	Fiscal year
GI	Gastrointestinal
HSC	Winnipeg Health Sciences Centre
ICD-9-C	International Classification of Diseases, Ninth Revision, Clinical Modification
ICD-10-CA	International Classification of Diseases, 10th Revision with Canadian Enhancements
IMV	Invasive mechanical ventilation
ICU	Intensive Care Unit
LTC	Long-term care
MCHP	Manitoba Centre for Health Policy
NPV	Negative predictive value
NNT	Number needed to treat
PCH	Personal Care Home
PPV	Positive predictive value
WICUDB	Winnipeg Intensive Care Unit Database

Executive Summary

Objective

This report was conducted by the Manitoba Centre for Health Policy (MCHP) on behalf of Manitoba Health and Seniors Care. Its major goal was to identify community-dwelling Manitobans, age 40 years and older, with a high risk in the near future (defined as 30-180 days from an Evaluation Date) of developing critical illness, defined as an acute, life-threatening medical condition.

Background and Relevance

The potential value of this effort derives from the importance of potentially avoidable critical illness. Care of critically ill people in Intensive Care Units (ICUs) is a large and expensive component of modern health care. In Canada, 11% of hospitalizations include time in ICUs, 19% of all deaths occur in them, and ICU use is increasing, having risen 12% from 2008 to 2012. In Manitoba, approximately 0.6% of adults are admitted to ICUs each year, with 17% of those people dying in hospital. The yearly Manitoba ICU admission rate increases with age, ranging from 0.3% to 12.0% across those aged 40-89 years. Additionally, many survivors suffer long-term adverse physical, cognitive, and psychological issues, reducing their quality of life and their ability to function and requiring high ongoing health system use.

Therefore, it would be an important step forward to be able to use readily available information to identify community-dwelling individuals with a high probability of developing critical illness in the near future. While investigators have attempted this in the past, they have met with limited success. We hypothesized that we could go further by applying advanced statistical methods to the data at MCHP. Specifically, we hypothesized that the longitudinal information about prior medical resource use would powerfully assist in identifying subgroups with high probability of near-future critical illness.

The ultimate value of being able to identify, in advance, even a significant minority of such individuals, is that it would then become practical to design and test interventions seeking to avoid or delay the onset of critical illness, which could be applied by medical practitioners in the outpatient setting.

Methods

The outcome of interest was a critical illness that occurred in the "near future", defined as 30-180 days after the Evaluation Date. Critical illness was defined as the presence of either of the following two events: (a) non-elective hospital admission that included care in a high-intensity ICU with use of artificial life support; or (b) non-palliative death, in or out of hospital.

AIM 1 (Chapter 2): Validation of Coding of Artificial Life Support

Three types of artificial life support are commonly used in ICUs: invasive mechanical ventilation (IMV) for respiratory failure, renal replacement therapies (RRT; dialysis) for kidney failure, and vasoactive drugs for cardiovascular failure. Because a need for artificial life support is part of our case definition of critical illness (Chapter 3), an important preliminary step in this project was to understand how the administrative data codes for these modalities compare with what actually occurs in ICUs. This was assessed for adults in Chapter 2 (Aim 1), where we compared those codes in the administrative hospital data (the Discharge Abstract Database, DAD) against the reference standard of information contained in the Winnipeg Intensive Care Unit Database (WICUDB).

We found that of the three forms of artificial life support assessed, only IMV was identified in the DAD with accuracy adequate for practical use. Specifically, the hospital data failed to identify use of vasoactive agents or RRT for numerous patients who actually received them.

Though direct identification in the DAD of intravenous vasoactive drugs and RRT were poor, overlap of use of those modalities with IMV was large, such that those on IMV also constitute a majority of individuals on vasoactive agents and acute RRT. Thus, going forward, we substituted the above-stated criterion of "with use of artificial life support" with "with use of invasive mechanical ventilation".

Aim 2 (Chapter 3): Main Methods and Findings

We created a statistical model attempting to predict near-future critical illness, i.e., 30-180 days after an Evaluation Date, which we took to be the first day of a given fiscal year (FY), i.e., April 1. We studied general population cohorts comprising individuals who as of an Evaluation Date were between 40 and 89 years old and residing in the community (including chronic care facilities).

We used Classification and Regression Tree (CART) analysis to identify subgroups of community-dwelling adults who experienced sufficiently high rates of near-future critical illness that it would be practical to intervene and attempt to avoid or delay the event. For this purpose, we chose a "practicality threshold" of intervening on no more than three people to have a chance of avoiding one outcome of a critical illness event, and we did this by identifying subgroups in which ≥33% of individuals would have the outcome.

CART uses input variables to divide all members of a cohort into mutually exclusive subgroups, each defined by a given value/range/category of each input variable. The result is a "tree" on which each "terminal leaf" is one such subgroup. To create such a tree, we used FY2013 and FY2014 data. We then evaluated its ability to predict future events in FY2015 data. We inputted 72 variables into the CART analysis, including: socio-demographic variables, comorbid diagnoses, degree of "rurality", living in a personal care home (PCH), utilizing homecare services, three readily available measures of frailty, and prior medical resource use. For types of medical resources used – including hospitals, outpatient visits, outpatient laboratory testing, and prescription medications – we used variables that allowed us to identify patterns of utilization during the two years prior to the Evaluation Date.

There were approximately 536,000 individuals included in each of the three years of data, of whom 0.38% experienced near-future critical illness. Of the 72 input variables, socioeconomic status had the highest importance in identifying the outcome, followed by living in a PCH. Frailty scores occupied the 3rd and 5th variable importance slots, and age was 6th.

In the data used to create it, the optimal tree performed well in identifying individuals with the outcome; 493 individuals were contained in 41 terminal leaves, each of which had ≥33% of its members experience the outcome. However, this performance was not reproduced when applying the same terminal leaf definitions to the future data, where these 41 leaves contained 429 individuals, but only 20 (4.7%) of them experienced the outcome.

Interpretation and Discussion

Although we leveraged the numerous variables and longitudinal nature of the data in the Manitoba Population Research Data Repository and the flexibility of CART analysis, we were not able to achieve the desired high-fidelity prediction of near-future critical illness among community-dwelling Manitobans. Among individuals identified by our analysis as being high-risk, only 5% actually developed it, instead of the desired value of at least 33%.

Nonetheless, there were some valuable observations from this work. The predictive importance of frailty was notable. Frailty is a syndrome of physiological decline characterized by vulnerability to adverse health outcomes. It is a construct that is distinct from (but associated with) age, comorbidity,

and health habits. It is possible to be frail without being elderly. It is also possible to be frail without any specific comorbid conditions. Frailty is associated with mortality and morbidity, and with the ability to benefit from aggressive medical interventions. Although other explanations are possible, the fact that frailty measures had relative importance almost three-fold higher than even the most influential specific chronic condition (metastatic cancer) is consistent with much of the influence of chronic conditions on future outcome being mediated by the frailty they cause, rather than the condition per se.

It appears that high fidelity prediction of near-future critical illness among community-dwelling adults will require including additional parameters. Variables not generally available in administrative data for entire populations may be necessary. These include innate biology, health behaviours, environmental exposures and other socioeconomic factors.

However, even though our predictive model's ability to identify individuals who develop near-future critical illness was lower than desired, further study of it may be warranted to assess whether alerting primary care providers to the existence of individuals on their patient rosters who have a 1 in 20 chance of near-future critical illness could reduce the rate of such events.

Chapter 1: Introduction

Introduction and Objective

This report was produced by the Manitoba Centre for Health Policy (MCHP) on behalf of Manitoba Health and Seniors Care. It used longitudinal, population-based data from the Manitoba Population Research Data Repository (the Repository) held at MCHP, covering nine fiscal years (April 1– March 31) 2007/08–2015/16.

Our goal was to identify community-dwelling Manitobans, age 40-89, with a high risk in the near future (defined herein as occurring between 30 and 180 days after a given date) of developing critical illness, defined as an acute, life-threatening medical condition. The report is organized into two aims. The first aim was to validate identification of use of artificial life support in hospital administrative data. The second aim was to use this validated definition to help create statistical models seeking to achieve the stated goal.

The potential value of this effort derives from the importance of potentially avoidable critical illness. Care of critically ill people in Intensive Care Units (ICUs) is a large [1–6] and expensive [1,2,4,7–12] component of modern health care. In Canada, 11% of hospitalizations include time in ICUs [1], 19% of all deaths occur in them [13], and ICU use is increasing, having risen 12% from 2008 to 2012 [1]. In Manitoba, approximately 0.6% of adults are admitted to ICUs each year [14]few such studies have been published. METHODS Population-based analysis of all adult ICU care in the Canadian province of Manitoba, 1999 to 2007, using administrative data. We calculated age-adjusted rates and trends of ICU care, overall and subdivided by age, sex and income. RESULTS In 2007, Manitoba had a population of 1.2 million, 118 ICU beds in 21 ICUs, for 9.8 beds per 100,000 population. Approximately 0.72% of men and 0.47% of women were admitted to ICUs yearly. The age-adjusted, male:female rate ratio was 1.75 (95% CI 1.64 to 1.88, with 9% of those dying in the ICU and 17% dying in hospital [15]. The yearly Manitoba ICU admission rate increases with age, and in the age group targeted in this study, it ranges from 0.3% to 12.0% [15]. Additionally, many survivors suffer long-term physical, cognitive and psychological problems that affect them adversely and require ongoing health system use [16].

Therefore, it would be an important step forward to be able to use readily available administrative data to identify community-dwelling individuals with a high probability of developing critical illness in the near future. While investigators have attempted this in the past, they have met with limited success [17–19]. We hypothesized that we could go further by applying

advanced statistical methods to the data in the Repository [20]. Specifically, we hypothesized that leveraging a range of socioeconomic indicators and longitudinal information about prior medical resource use would powerfully assist in identifying subgroups with high probability of near-future critical illness or death.

The ultimate value of being able to prospectively identify even a significant minority of such individuals is that it would then become practical for researchers to design and test interventions seeking to avoid or delay the expected adverse health event, which could then be applied by medical practitioners in the outpatient setting.

General Methods

All data management, programming and analyses were performed using SAS® version 9.2 and SAS Enterprise Miner version 13.5. The data used in this analysis are derived from records that are primarily collected to administer the universal healthcare system within Manitoba. The Repository contains information of key interest to health planners and includes de-identified person-level data such as birth date and mortality, contacts with physicians and hospitals, pharmaceutical dispensing, use of home care services and personal care homes (PCHs), as well as area-level data such as average household income by dissemination area from the Canada Census.

The following database files were used for analyses in this report. Detailed information is available on the MCHP website at: http://umanitoba.ca/faculties/health_sciences/medicine/units/chs/departmental_units/mchp/resources/repository/descriptions.html.

- **Manitoba Health Insurance Registry** - for data about the time a person is registered as a resident of Manitoba, as well as their date of birth [age], sex, area of residence, and marital status
- **Vital Statistics Mortality** - for deaths and causes of death
- **Medical Services** - for visits to physicians outside of hospitals
- **National Rehabilitation Reporting System** - for time spent in rehabilitation facilities
- **Social Allowances Management Information Network (SAMIN)** - to identify social assistance
- **Provider Registry** - to identify the type of medical service provider
- **Hospital Abstracts** - for hospital discharges
- **Drug Program Information Network (DPIN) data** - for prescriptions dispensed from community-based pharmacies
- **Critical Care/Intensive Care Database** (referred to in this report as the Winnipeg Critical Care Database, WICUDB)
- **Manitoba Renal Program** - to identify people on chronic renal dialysis
- **Diagnostic Services Manitoba** - for outpatient clinical laboratory testing
- **Health Links** – Info Santé - for after-hour calls seeking medical information
- **Home Care (including the Home Care MDS assessment and the PROCURA database)** - for use of home care both provincially and in the Winnipeg Regional Health Authority
- **Long-Term Care Utilization** - for the use of long-term care facilities
- **Public Use Census files** - for neighbourhood-level income quintile information

Two additional notes are in order:

1. Throughout this document, rates were suppressed (that is, not reported) where the counts upon which the rates are based represent five or fewer events (unless the rate is truly 0, in which case it can be reported). This is to avoid breeches of confidentiality and is similar to the way Statistics Canada reports data. Throughout the report, the letter “s” indicates suppressed data.
2. Unless otherwise specified, year(s) refers to fiscal year(s) (April 1 to March 31).

Chapter 2:
Aim 1: Using Administrative Data to Validate Identification of Use of Artificial Life-Supporting Modalities in Intensive Care Units

Aim

To assess, in adult ICU patients 40-89 years old, the accuracy of hospital administrative data for identifying use in ICU of the three most common forms of artificial life support: invasive mechanical ventilation (IMV), intravenous vasoactive drugs, and acute renal replacement therapy (acute RRT). This is relevant to the main purpose of this work, in that need for artificial life support is part of our case definition of critical illness (Chapter 3).

Key Findings

- Of the three most common forms of artificial life support, only IMV is identified in the hospital Discharge Abstract Data (DAD) with accuracy adequate for practical use.
- Though direct identification in the DAD of intravenous vasoactive drugs and acute RRT were poor, overlap of use of those modalities with IMV was large.
- Due to this large overlap, identifying those who received IMV captured 81% of all individuals who received any of the three modalities of artificial life support.

Methods

This aim used Repository data for the five years 2007/08-2011/12. The reference standard for use of life support modalities was the WICUDB, which contains clinical data about all adult ICU admissions in the Winnipeg Health Region since 1999. During the study period there were 11 adult ICUs within six hospitals in the region. The types of ICUs were: five medical-surgical, one medical, one general surgical, one cardiac surgical, two coronary care, and one respiratory. Data in the WICUDB are obtained from manual record review by specially-trained former ICU nurses dedicated to this data collection. It includes daily information about use of: (i) IMV, (ii) any intravenous vasoactive agents, and (iii) RRT, the latter categorized as intermittent hemodialysis, continuous hemodialysis, or peritoneal dialysis. We used the Manitoba Renal Program Chronic Dialysis Registry to identify individuals who underwent chronic outpatient dialysis (hemodialysis or peritoneal dialysis) [21]specificity, predictive value and overall accuracy of 4 administrative case definitions for the diagnosis of ESRD requiring chronic dialysis over different time horizons from Jan. 1, 2004, to Mar. 31, 2011. The Manitoba Renal Program Database served as the gold standard for confirming dialysis status. RESULTS During the study period, 2562 patients were registered as recipients of chronic dialysis in the Manitoba Renal Program Database. Over a 1-year period (2010. We categorized the listed primary ICU admission diagnosis into 19 groups, adapted from International Classification of Disease (ICD)-10-CA chapter headings [22].

We used the DAD to identify life support modalities.[1] The DAD includes up to 25 diagnosis codes in ICD-10-CA, and up to 20 procedure codes coded according to the Canadian Classification of Health Interventions (CCI) [23]. While quality testing on DAD data has demonstrated abstraction-reabstraction reliability of 94% for IMV and 97% for RRT [24], this does not speak to the validity of the DAD for identifying these interventions. Discharge abstracts have excellent accuracy for identifying the existence and timing of ICU care during hospitalization [25]. Use of IMV, vasoactive agents, and RRT in the DAD are indicated by specific CCI procedure codes (See definition 1 in Appendix Table 1.1). CCI codes indicating mechanical ventilation by endotracheal tube or tracheostomy were used for IMV. The only relevant CCI code for vasoactive agents is use of “cardiac stimulants”, defined specifically as any of epinephrine, dopamine, dobutamine, amrinone or isoproterenol; norepinephrine is not included. For RRT, we used CCI codes representing intermittent or continuous hemodialysis, excluding peritoneal dialysis, as it is virtually never used as an acute, new-onset renal replacement modality.

The unit of measure for this part of the analysis was the ICU-containing hospital abstract. An abstract was included if the WICUDB indicated the person was age 40 years or older and admitted to any of the 11 Winnipeg adult ICUs with discharge dates during the five-year study period. In comparison with the WICUDB, we calculated sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and overall accuracy of the DAD for identifying the three forms of artificial life support. Exact binomial confidence intervals were used to calculate the 95% confidence intervals around these values. Given the overall goal of this work, we were more needful of avoiding falsely-positive identifications of use of life-supporting medical therapies than of avoiding falsely-negative ones. Thus, we recognized a priori the need for a PPV>90% for administrative data definitions to be useful in our identification of critical illness (Chapter 3).

In sensitivity analyses, we modified the administrative data definitions of the forms of life-supporting medical therapies (Appendix Table 1.1, definitions 2 and 3). For IMV, we: (a) added procedure codes to include those for intubation and tracheostomy, and (b) excluded patients admitted to the cardiac surgical ICU, because all patients undergoing open-heart surgery in Manitoba are admitted to that unit, almost all being transferred there on IMV. For RRT, we: (a) added procedure codes for placement of a hemodialysis catheter, (b) added ICD-10-CA diagnosis codes for acute renal failure, and (c) excluded patients on chronic dialysis of any type, identified from the Manitoba Renal Program Chronic Dialysis Registry. For vasoactive agents, we added ICD-10-CA codes for shock.

Results

Over the five-year study period, there were 20,764 ICU-containing hospitalizations involving 17,624 unique, eligible people. Characteristics of the hospitalizations at ICU admission are shown in Table 2.1.

As shown in Table 2.2[2], per the WICUDB reference standard, IMV was used in 52.6% of eligible ICU-containing hospitalizations. Identification of IMV in hospital abstracts was excellent, with sensitivity, specificity, PPV and NPV all exceeding 90%. Including procedure codes for intubation or tracheostomy did not improve on the definition using only IMV procedure codes. Excluding the cardiac surgery patients had little effect on performance.

Intravenous vasoactive agents were used in 46.8% of eligible ICU-containing hospitalizations. The CCI procedure code for use of the selected set of vasoactive drugs was never listed in the DAD records for these hospitalizations. Adding diagnosis codes for shock to the procedure code led to a large number of false negative identifications of use of these agents, with a PPV of 86% and a NPV of 59%.

1 The hospital DAD are abstracted by centrally trained personnel from medical charts in each hospital, using uniform definitions, data collection standards [74,75], and data entry software with established quality assurance methodologies. [76] DAD elements and format are mandated by the Canadian Institute for Health Information [77].

2 See Appendix Tables 1.2 to 1.11 for contingency tables comparing administrative data definitions for the three types of life-supporting medical therapies.

Table 2.1: Characteristics of Included Hospitalizations

Variable	Value
Number of Intensive Care Unit (ICU)-containing hospital abstracts	20,764
Age, years	
mean ± SD	66.1 ± 12.6
median (interquartile range)	66 (57, 76)
Female, n (%)	8,004 (38.6)
Acute Physiology and Chronic Health Evaluation (APACHE) II score	
mean ± SD	16.3 ± 7.9
median (interquartile range)	15 (11, 21)
APACHE II Acute Physiology Score	
mean ± SD	9.8 ± 5.5
median (interquartile range)	9 (6, 13)
ICU type, n (%)	
Tertiary hospital, medical	2,331 (11.2)
Tertiary hospital, surgical	1,630 (7.9)
Tertiary hospital, medical-surgical	2,297 (11.1)
Two tertiary hospitals, coronary care	3,874 (18.7)
Tertiary hospital, cardiac surgical	4,418 (21.3)
Tertiary hospital, respiratory	26 (0.1)
Four community hospitals, medical-surgical	6,188 (29.8)
ICU admission diagnosis category, n (%)	
Cardiac	10,281 (49.5)
Endocrine	111 (0.5)
Ear, nose and throat	145 (0.7)
Genitourinary	23 (0.1)
Gastrointestinal	1,126 (5.4)
Hematologic	36 (0.2)
Infection	961 (4.6)
Metabolic	44 (0.2)
Musculoskeletal/Skin and Soft Tissue	144 (0.7)
Neoplasia	41 (0.2)
Neuropsychiatric	1,143 (5.5)
Obstetric	60 (0.3)
Poisoning/Overdose	480 (2.3)
Renal	174 (0.8)
Respiratory	5,009 (24.1)
Trauma	384 (1.9)
Vascular	414 (2.0)
Others	188 (0.9)
ICU length of stay, days	
mean ± SD	6.2 ± 12.7
median (interquartile range)	3 (2, 6)
ICU mortality, n (%)	2,412 (11.6)
Hospital mortality, n (%)	3,467 (16.7)

RRT was used during 4.4% of all eligible ICU-containing hospitalizations, and 2.9% when excluding individuals on chronic renal dialysis. While the primary administrative data definition of procedure codes for hemodialysis had a sensitivity and specificity exceeding 92%, due to the low prevalence of RRT, the PPV was just 55.4%. Adding procedure codes for dialysis catheter placement did not improve on the administrative definition that used only procedure codes for the hemodialysis itself. Additionally, adding diagnosis codes for acute renal failure very slightly improved the sensitivity and negative predictive values, but at the expense of reduced specificity (declined from 96.6 to 86.7%) and PPV (declined from 55.4 to 24.4%). The exclusion of chronic dialysis patients from the cohort did not appreciably alter the performance of the administrative case definition.

Table 2.2: Performance of Administrative Data Definitions for the Three Types of Life-Supporting Medical Therapies

Hospital Abstract Definition	Count	Prevalence* (%)	Sensitivity (%, 95% CI)	Specificity (%, 95%CI)	Positive Predictive Value (%, 95%CI)	Negative Predictive Value (%, 95% CI)	Accuracy (%, 95% CI)
Invasive Mechanical Ventilation (IMV)							
Procedure codes for IMV (primary definition**)	20,764	52.6	91.5 (91.0-92.0)	94.5 (94.0-94.9)	94.8 (94.4-95.2)	91.0 (90.4-91.5)	92.9 (92.6-93.3)
Procedure codes for IMV OR intubation OR tracheostomy	20,764	52.6	91.7 (91.2-92.2)	94.4 (94.0-94.9)	94.8 (94.4-95.2)	91.1 (90.6-91.7)	93.0 (92.7-93.3)
Procedure codes for IMV, excluding cardiac surgical patients	15,736	51.1	90.7 (90.1-91.3)	96.5 (96.1-96.9)	96.4 (96.0-96.9)	90.8 (90.2-91.4)	90.8 (90.2-91.4)
Intravenous Vasoactive Agents (Vasoactive Agents)							
Procedure code for vasoactive agents (primary definition)	20,764	46.8	0.0 (0.0-0.0)	100.0 (100.0-100.0)	undefined	53.2 (52.5-53.9)	53.2 (52.5-53.9)
Procedure code for vasoactive agents OR diagnosis codes for shock	20,764	46.8	23.3 (22.5-24.2)	96.6 (96.2-96.9)	85.7 (84.4-87.0)	58.9 (58.1-59.6)	62.3 (61.6-62.9)
Acute Renal Replacement Therapy (RRT)							
Procedure codes for hemodialysis (primary definition)	20,764	4.4	92.2 (90.4-93.9)	96.6 (96.4-96.9)	55.4 (52.9-57.9)	99.6 (99.6-99.7)	96.4 (96.2-96.7)
Procedure codes for hemodialysis OR hemodialysis catheter insertion	20,764	4.4	92.3 (90.6-94.0)	96.2 (96.0-96.5)	52.8 (50.4-55.3)	99.6 (99.6-99.7)	96.1 (95.8-96.3)
Procedure codes for hemodialysis OR hemodialysis catheter insertion OR diagnosis codes for acute renal failure	20,764	4.4	94.5 (93.0-96.0)	86.7 (86.2-87.1)	24.4 (23.0-25.9)	99.7 (99.6-99.8)	87.0 (86.5-87.5)
Procedure codes for hemodialysis, excluding chronic dialysis patients	20,204	2.9	92.9 (90.8-95.0)	97.2 (96.9-97.4)	49.1 (46.1-52.1)	99.8 (99.7-99.9)	97.0 (96.8-97.3)
Any one or More of IMV, Vasoactive Agents or RRT							
Case Definitions for any 3 types of life support	20,764	65.7	78.0 (77.3-78.7)	94.7 (94.2-95.2)	96.6 (96.2-96.9)	69.3 (68.3-70.2)	83.7 (83.2-84.2)

* Prevalence derived from the reference standard of the Winnipeg Intensive Care Unit Database
** See Appendix Table 1.1 for definitions

Among all ICU-containing hospitalizations, any one or more of the three life support modalities was used while in ICU for 13,633 (65.7%) individuals (Figure 2.1). Overlapping use of the three types of life-supporting medical therapies was substantial. Among individuals who received any one of the three types, 68-76% received at least one of the two other types (Table 2.3 and Appendix Table 1.11). In particular, IMV was applied to 75% of those who received vasoactive agents, and 59% of those who received RRT.

Figure 2.1: Overlapping Use of Life-Supporting Medical Therapies in the Total Cohort, Based on the Reference Standard
Number of hospital abstracts in each segment is shown in parentheses

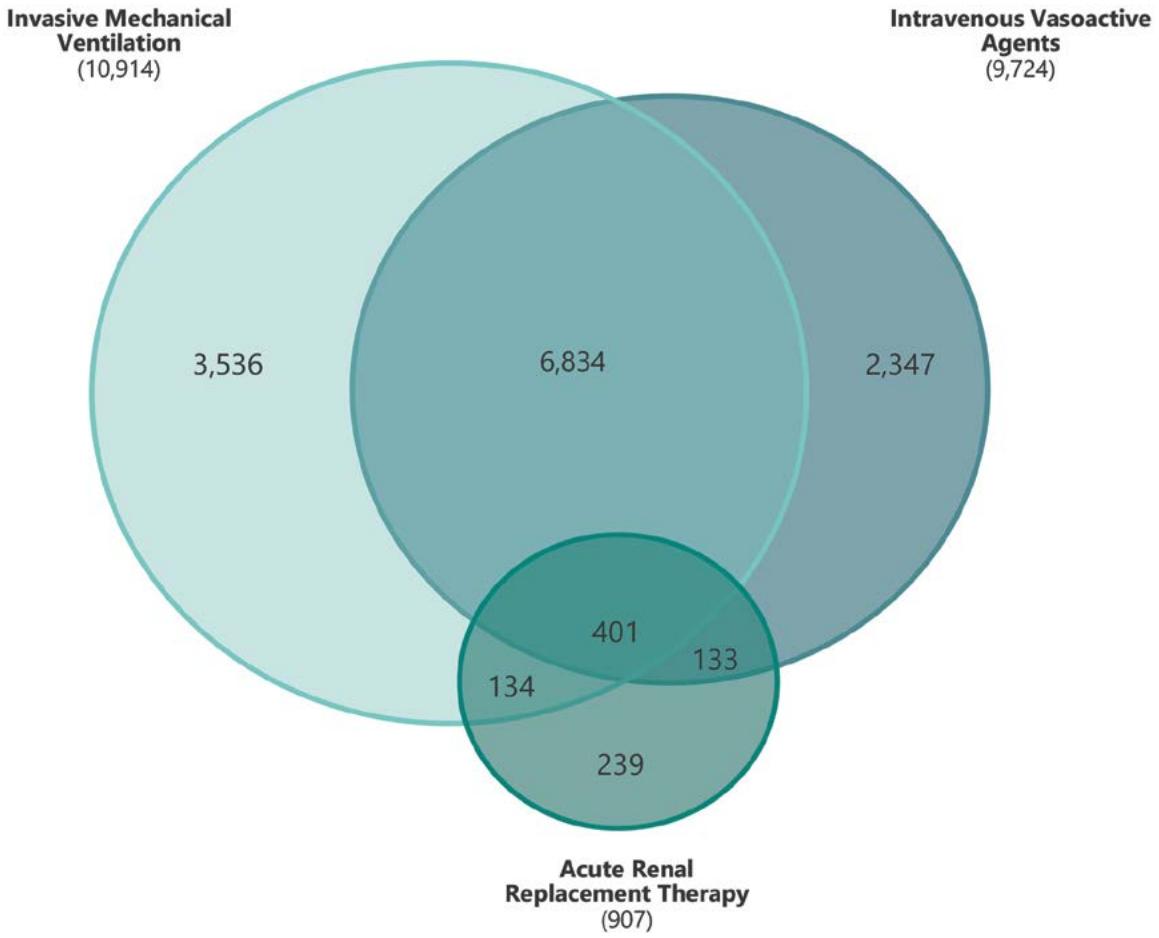

Table 2.3: Overlapping Use of Life-Supporting Medical Therapies in the Total Cohort, Based on the Reference Standard

	IMV*	Vasoactive Agents*	RRT*	IMV or Vasoactive agents	IMV or RRT	Vasoactive agents or RRT
IMV: n=10,914	-	7,244 (66.4%)	535 (4.9%)	-	-	7,378 (67.6%)
Vasoactive Agents: n=9,724	7,244 (74.5%)	-	534 (5.5%)	-	7,377 (75.9%)	-
Acute RRT: n=907	535 (59.0%)	534 (58.9%)	-	668 (73.7%)	-	-

*IMV - invasive mechanical ventilation; vasoactive agents - intravenous vasoactive agents; RRT - acute renal replacement therapy

Chapter 3:
Aim 2: Identifying Community-Dwelling People with a High Probability of Developing Critical Illness in the Near Future

Aim

To develop and evaluate the ability of predictive modeling to prospectively identify subgroups of community-dwelling (which herein includes those residing in personal care homes (PCHs)) Manitobans with a high (≥33%) probability of developing critical illness in the near future.

Key Findings

- We applied Classification and Regression Tree (CART) analysis to data from fiscal years (FY) 2013 to 2015, divided into a training dataset (to create the tree) and a test dataset (to evaluate its performance on 'future' data).
- 72 variables were included in the analysis, including: socio-demographic factors, home care use, living in or panelled for a PCH, comorbid chronic conditions, longitudinal assessment over 24 months of six types of medical resource use, most recent use of four additional medical interventions, and measures of frailty.
- Approximately 536,000 individuals were included in each of the three years of data, 0.38% of whom experienced the outcome of a near-future critical illness.
- The final CART tree had 21 branching levels and 2,644 terminal leaves (subgroups). Socioeconomic status, living in a PCH, frailty and age were among the input variables with the highest importance in identifying people with high risk of developing critical illness in the near future.
- In the training data, the final tree performed well in identifying individuals with a critical illness; 493 individuals each of whom had ≥33% risk of the outcome, were identified. However, this performance was not reproduced in the test dataset; of 429 individuals identified, only 4.7% of them had the outcome.

Methods

This analysis was performed using yearly cohorts. For each year, 2013 to 2015, we considered April 1 (the start of the FY) to be the "Evaluation Date", and used data going back two years prior in attempting to identify subgroups with high rates of critical illness in the 30-180 days following the Evaluation Date.

Outcome Definition

The outcome of interest was a critical illness that occurred in the "near future", defined as 30-180 days after the Evaluation Date. Thirty days was chosen as the lower limit because it would require some time to locate, contact, and engage the individual in an intervention seeking to avoid the adverse outcome. The upper limit of 180 days provides sufficient time for events to occur, while expecting that the ability to predict future health events would degrade further with the passage of time after the Evaluation Date.

Critical illness was defined as the presence of either of the following two events:

(a) non-elective hospital admission that included care in a high-intensity ICU with use of invasive mechanical ventilation; OR

(b) non-palliative death, in or out of hospital.

The Critical Illness Date for an individual who experienced this outcome during the 30-180 day follow-up interval after an Evaluation Date was when the first of these event occurred.

We used the Admission Type field of DAD records to exclude elective hospital admissions. High-intensity ICUs are those capable of providing artificial life support for an unlimited period; the only high-intensity ICUs in Manitoba are the adult ICUs in the Winnipeg Regional Health Authority (except the intermediate ICU at HSC) and the medical-surgical ICU in Brandon[3]. Rather than including ICU admissions with use of any type of artificial life support, based on the findings of Aim 1 (Table 2.1), we limited our focus to ICU-containing DAD records that included procedure codes for invasive mechanical ventilation.

Yearly Cohort Inclusion and Exclusion Criteria

The study cohorts were general population cohorts comprising individuals who at the Evaluation Date were: (a) between 40 and 89 years old; and (b) continuously registered with Manitoba Health from two years before the Evaluation Date to either one year after the Evaluation Date, or the Critical Illness Date (if it occurred), whichever occurred first.

We applied several exclusion criteria to the cohorts, which are described here, along with the rationale for exclusion:

1. Individuals who had a newly diagnosed malignancy within the five years before the Evaluation date.

   Rationale: ICU admission and death due to cancers are common [15,26], and our ultimate goal is to design interventions to avoid or delay critical illness or death. Thus, as undiagnosed cancers are rare [27,28], critical illness (including death) from cancer is unlikely to be avoidable, although we acknowledge that identifying near-future critical illness in persons with cancer could provide the opportunity for a different intervention such as proactively transitioning them to palliative care. The choice of five years was made since five-year survival is a common benchmark for long-term survival in those with malignancy. We followed Lix et al.'s [29] approach to identify malignancies; this approach is described following these exclusion criteria. The approach to identifying cancer is described further below.

2. Individuals in an acute care hospital on the Evaluation Date.

   Rationale: Our goal was to identify individuals residing in the community who were presumably medically stable when they developed the outcome.

3. Individuals who were in the chronic care sections of Riverview Health Centre or Deer Lodge Centre on the Evaluation Date. We identified these individuals using the long-term care (LTC) database, as codes 6 or 7, with facility codes for the portions of those two facilities that are distinct from the facility codes for the attached PCHs.

   Rationale: Our goal was to identify individuals residing in the community who were presumably medically stable at least 30 days prior to developing the outcome. The excluded portions of these two facilities differ from usual PCHs in housing individuals with ongoing acute medical conditions, such as prolonged respiratory failure requiring mechanical ventilation.

3 During the period of this study, these included: (a) in Winnipeg, five medical-surgical ICUs, one medical ICU, one surgical ICU, one cardiac surgical ICU and two coronary care units, and (b) in Brandon, a single medical-surgical-cardiac ICU.

4. Individuals enrolled in an identified palliative care program during the prior two years, identified as having experienced any of the following during the two years before the Evaluation Date: (i) being in palliative care in any Manitoba hospital, indicated by hospital diagnosis codes (ICD-9-CM code V66.7, ICD-10-CA code Z51.5); (ii) the palliative care service had primary responsibility for hospital care, as indicated in the DAD; (iii) received outpatient palliative care as indicated by the presence of palliative care codes in the home care database; or (iv) received outpatient palliative care as indicated in the DPIN database of medication payment under the palliative care program.

   Rationale: Such individuals are expected to have a short life expectancy and would be much less likely to seek curative medical care at the end of life.

5. Index hospitalizations with ICU care were for trauma or injury, defined by DAD records with ICD-10 diagnosis codes: S00-T35, T66-T79, V, W, or X, that were of diagnosis types indicating that they were present on hospital admission, i.e., Type 1 OR Type 5 OR Type M without also being listed as Type 2 OR Type 6 without also being listed as Type 2.

   Rationale: Trauma and injury are very different from medical illnesses, and we expected that they would be much more difficult to predict or prevent.

As noted above, we followed Lix et al.'s approach of using diagnosis codes to identify malignant cancers, who showed that for the five most common cancers, a single inpatient or outpatient ICD-9 or ICD-10 diagnosis code has excellent accuracy [29]. We followed Quan et al. [30]10th Revision (ICD-10 in identifying diagnosis coding for malignancies.[4] To identify whether a malignancy was first diagnosed within the five years before a given date, we identified any malignancy codes that appeared in DAD records or outpatient claims for the five years before the Evaluation Date but did not appear 5-10 years prior.

Analysis

As described in more detail in Appendix 2, we used Classification and Regression Tree (CART) analysis to identify subgroups of community-dwelling adults who experienced high rates of near-future critical illness [31,32].

CART uses input variables to divide all members of a cohort into mutually exclusive subgroups, each defined by a given value/range/category of each input variable. The result is a "tree" where each "terminal leaf" is one such subgroup. To create and identify the best predicting tree, CART utilizes two distinct datasets, termed the training and validation datasets. We combined the FY2013 and FY2014 cohorts, and then randomly subdivided them, 60:40, into training and validation cohorts. We then assessed how this model performed on the 2015 cohort (the test cohort). One measure of performance used was lift, which measures performance of a tree at predicting events in a chosen subset of leaves, compared to the rate of events in the entire sample. Lift equals the outcome rate in the subset divided by the rate in the entire population; e.g., if the rate of events in the entire population is 1%, but in a given subset of leaves the rate is 20%, then the lift for this subset is 20.

We chose to use CART for three reasons. First, we expected that identifying a substantial number of individuals who would develop critical illness in the near future would require finding a large number of diverse subgroups (represented by terminal leaves) in which ≥33% experienced the outcome. Such subgroups would require applying an eventual intervention to no more than three people to have a chance to avert or delay one episode of critical illness. Second, we expected that the longitudinal health data contained in the Repository would be critical to our goal of predicting near-future critical illness. Specifically, we hypothesized that there would be temporal patterns of health care resource use associated with higher risk of the outcome. We chose a priori a time interval of 24 months before an Evaluation Date, which we divided into four intervals: (A) months 1-12, (B) months 12-18, (C) months 19-21 and (D) months 22-24, which is the most recent three-month period. The flexibility of CART allows it to include counts from different intervals to relate the outcome to temporal patterns of resource use. We entered 72 variables into CART, measured as of the Evaluation Date, unless otherwise indicated (Table 3.1; see Appendix 2 for detailed definitions). Finally, CART provides more easily understood subgroup separation than do more commonly used prediction methods such as logistic regression.

4 ICD-9 codes: 140.x-165.x, 170.x-176.x, 179.x-195x, 200.x-208.x; ICD-10 codes: C00.x-C26.x, C30.x-C34.x, C37.x-C38.x, C41.x, C43.x -C58.x, C60.x-C76.x, C81.x-C86.x, C88.x, C90.x-C96.x.

Table 3.1: Input Variables for Classification and Regression Tree Analysis

Variable	Details
Age	continuous
Biologic sex	binary
Socioeconomic status as SEFI-2 score [66]	continuous
Ever received income assistance	binary
Statistical Area Classification [67]	ordinal, 6 categories
Distance from residence to closest intensive care unit (ICU)	continuous, closer of Winnipeg or Brandon
Open Home Care file	binary
Panelled for personal care home placement	binary
Living in a personal care home	binary
Chronic comorbid diagnoses (Elixhauser comorbidities)	31 binary variables
Dementia	binary
Frailty, per measure of Segal et al. [39]	continuous, ranges 0-1
Frailty, per measure of McIsaac et al. [40]	continuous, ranges 0-30
Frailty, per Johns Hopkins ACG® Case-Mix System [70]	binary
Timing of most recent ICU admission	5 categories*
Timing of most recent cardiac catheterization	5 categories*
Timing of most recent gastrointestinal endoscopy	5 categories*
Timing of most recent bronchoscopy	5 categories*
# Acute hospital days	4 separate continuous variables**
# Days designated as "Alternate Level of Care" in a hospital, or spent in a rehabilitation facility	4 separate continuous variables**
# Outpatient clinic (physician, nurse practitioner and primary care nurse) visits	4 separate continuous variables**
# Days with calls made to Health Links – Info Santé	4 separate continuous variables**
# Outpatient laboratory tests	4 separate continuous variables**
# Categories of prescription medications dispensed	4 separate continuous variables**

Note: See Appendix 1 for the technical definitions of these variables.
Note: Numbers in square brackets refer to references in the Reference List
* 0-1 month prior, 2-6 months prior, 7-12 months prior, 13-24 months prior, or >24 months prior/never
** Four variables, representing counts during 4 intervals before the Evaluation Date: (A) 13-24 months prior, (B) 7-12 months prior, (C) 4-6 months prior, and (D) 0-3 months prior

Results

Subject Characteristics and Input Variables

Table 3.2 describes the patients included in this analysis. Approximately 536,000 individuals were included in each of the three years of data. In each of the training, validation, and test datasets, 0.38% of individuals experienced the outcome. Approximately one-quarter of these individuals experienced ICU admission with IMV, while the other three-quarters experienced non-palliative death without ICU admission. Not unexpectedly, every one of the 72 variables inputted to the CART analysis differed significantly between those who did and did not experience the outcome. While the large sample sizes used can assign statistical significance to small absolute differences, for most of these parameters the differences were substantial in absolute terms.

For example, people with the outcome were 2.4-7.5 times more likely to have had ICU care, cardiac catheterization, gastrointestinal (GI) endoscopy and bronchoscopy within the 1 month before the Evaluation Date. They were 10-20 times more likely to live in a PCH or to have an open home care file. They were more than twice as likely to have frailty scores in the highest tercile. In the month prior to the Evaluation Date, people with the outcome had, on average, 4.4 more hospital days, 0.8 more outpatient visits, 0.9 more outpatient laboratory tests, and they filled prescriptions for 3.2 additional classes of drugs compared to individuals without the outcome.

Table 3.2: Characteristics of the Individuals in the Datasets Used for CART Analysis

Values are counts (%) unless indicated otherwise

Variables	Training/Validation Data 2013/14-2014/15 # with outcome = 4,065 (0.38%)			Test Data 2015/16 # with outcome = 2,044 (0.38%)		
	No Outcome	p-value	With Outcome	No Outcome	p-value	With Outcome
Total N	1,060,252	-	4,065	541,703	-	2,044
Outcome breakdown:						
Intensive care unit (ICU) admission with IMV only	-	-	649 (16.0)	-	-	380 (18.6)
Non-palliative death only	-	-	3,145 (77.4)	-	-	1,529 (74.8)
Both*	-	-	271 (6.7)	-	-	135 (6.6)
Age (years)						
40-44	154,117 (14.5)	<.0001	63 (1.6)	77,786 (14.4)	<.0001	44 (2.2)
45-49	161,566 (15.2)		129 (3.2)	78,277 (14.5)		57 (2.8)
50-54	174,946 (16.5)		221 (5.4)	88,351 (16.3)		109 (5.3)
55-59	156,373 (14.8)		296 (7.3)	80,164 (14.8)		158 (7.7)
60-69	228,638 (21.6)		820 (20.2)	121,610 (22.5)		387 (18.9)
70-79	119,940 (11.3)		983 (24.2)	63,195 (11.7)		525 (25.7)
80-89	64,672 (6.1)		1,553 (38.2)	32,320 (6.0)		764 (37.4)
Female	544,620 (51.4)	<.0001	1,797 (44.2)	277,581 (51.2)	<.0001	894 (43.7)
Socioeconomic status (SEFI-2; octiles)						
Lowest (-5.2 to -1.1)	132,693 (12.5)	<.0001	323 (8.0)	67,814 (12.5)	<.0001	140 (6.9)
2nd (-1.0 to -0.68)	132,829 (12.5)		338 (8.3)	67,796 (12.5)		201 (9.8)
3rd (-0.67 to -0.43)	132,447 (12.5)		443 (10.9)	67,740 (12.5)		207 (10.1)
4th (-0.42 to -0.22)	132,853 (12.5)		602 (14.8)	67,409 (12.4)		296 (14.5)
5th (-0.21 to 0.02)	132,394 (12.5)		474 (11.7)	67,859 (12.5)		255 (12.5)
6th (0.03 to 0.24)	132,230 (12.5)		588 (14.5)	67,811 (12.5)		291 (14.2)
7th (0.25 to 0.67)	132,478 (12.5)		596 (14.7)	67,649 (12.5)		300 (14.7)
Highest (0.68 to 3.88)	132,328 (12.5)		701 (17.2)	67,625 (12.5)		354 (17.3)
Ever received income assistance	107,133 (10.1)	<.0001	600 (14.8)	56,795 (10.5)	<.0001	336 (16.4)

Note: IMV - invasive mechanical ventilation

Note: See Appendix 1 for the technical definitions of these variables.

*For individuals who experienced both elements of the outcome, the outcome timing was taken as the ICU admission.

Table 3.2. Cont'd: Characteristics of the Individuals in the Datasets Used for CART Analysis
Values are counts (%) unless indicated otherwise

Variables	Training/Validation Data 2013/14-2014/15 # with outcome = 4,065 (0.38%)			Test Data 2015/16 # with outcome = 2,044 (0.38%)		
	No Outcome	p-value	With Outcome	No Outcome	p-value	With Outcome
Statistical Area Classification						
Census Metropolitan Area	661,405 (62.4)	<.0001	2,474 (60.9)	338,647 (62.5)	0.0322	1,259 (61.6)
Census Agglomerations	100,224 (9.5)		351 (8.6)	51,169 (9.5)		180 (8.8)
Strong metropolitan influenced zone (MIZ)	60,696 (5.7)		200 (4.9)	31,806 (5.9)		97 (4.8)
Moderate MIZ	122,798 (11.6)		507 (12.5)	62,136 (11.5)		276 (13.5)
Weak MIZ	98,286 (9.3)		440 (10.8)	49,455 (9.1)		199 (9.7)
No MIZ	16,804 (1.6)		92 (2.3)	8,478 (1.6)		33 (1.6)
Distance from residence to closest ICU, octiles (km)**						
Shortest (0-1.60)	132,271 (12.5)	<.0001	741 (18.2)	67,572 (12.5)	<.0001	396 (19.4)
2nd (1.61-2.60)	132,557 (12.5)		506 (12.5)	67,670 (12.5)		304 (14.9)
3rd (2.61-3.49)	132,568 (12.5)		434 (10.7)	67,782 (12.5)		199 (9.7)
4th (3.50-4.54)	132,650 (12.5)		428 (10.5)	67,746 (12.5)		201 (9.8)
5th (4.55-13.1)	132,602 (12.5)		438 (10.8)	67,680 (12.5)		195 (9.5)
6th (13.2-47.4)	132,037 (12.5)		420 (10.3)	67,823 (12.5)		225 (11.0)
7th (47.4-97.0)	133,114 (12.6)		506 (12.5)	67,662 (12.5)		248 (12.1)
Farthest (97.1-1000)	132,453 (12.5)		592 (14.6)	67,768 (12.5)		276 (13.5)
Open Home Care file	11,469 (1.1)	<.0001	443 (10.9)	5,780 (1.1)	<.0001	227 (11.1)
Panelled for personal care home placement	583 (0.1)	<.0001	15 (0.4)	206 (0.0)	<.0001	8 (0.4)
Lives in a personal care home	9,233 (0.9)	<.0001	761 (18.7)	4,264 (0.8)	<.0001	343 (16.8)

Note: See Appendix 1 for the technical definitions of these variables.
**Distance between residence and closer of Winnipeg or Brandon

Table 3.2. Cont'd: Characteristics of the Individuals in the Datasets Used for CART Analysis
Values are counts (%) unless indicated otherwise

Variables	Training/Validation Data 2013/14-2014/15 # with outcome = 4,065 (0.38%)			Test Data 2015/16 # with outcome = 2,044 (0.38%)		
	No Outcome	p-value	With Outcome	No Outcome	p-value	With Outcome
Elixhauser comorbidities						
Hypertension without complications	347,428 (32.8)	<.0001	2,419 (59.5)	189,505 (35.0)	<.0001	1,311 (64.1)
Depression	232,502 (21.9)	<.0001	1,132 (27.9)	120,653 (22.3)	<.0001	586 (28.7)
Rheumatoid arthritis/CVD	187,681 (17.7)	<.0001	840 (20.7)	98,191 (18.1)	<.0001	454 (22.2)
Diabetes mellitus without complications	146,011 (13.8)	<.0001	1,286 (31.6)	78,753 (14.5)	<.0001	721 (35.3)
Chronic pulmonary disorders	126,858 (12.0)	<.0001	1,107 (27.2)	68,258 (12.6)	<.0001	550 (26.9)
Hypothyroidism	74,779 (7.1)	<.0001	420 (10.3)	40,957 (7.6)	<.0001	215 (10.5)
Cardiac arrythmia	41,327 (3.9)	<.0001	809 (19.9)	21,582 (4.0)	<.0001	408 (20.0)
Deficiency anemia	31,376 (3.0)	<.0001	351 (8.6)	19,401 (3.6)	<.0001	204 (10.0)
Obesity	29,413 (2.8)	<.0001	189 (4.7)	15,654 (2.9)	<.0001	105 (5.1)
Other neurologic disorders	27,274 (2.6)	<.0001	453 (11.1)	14,521 (2.7)	<.0001	226 (11.1)
Congestive heart failure	24,988 (2.4)	<.0001	917 (22.6)	12,649 (2.3)	<.0001	414 (20.3)
Drug abuse	23,822 (2.3)	<.0001	135 (3.3)	11,165 (2.1)	<.0001	70 (3.4)
Cancer without metastases	22,118 (2.1)	<.0001	368 (9.1)	11,567 (2.1)	<.0001	188 (9.2)
Peripheral vascular disease	21,862 (2.1)	<.0001	433 (10.7)	11,383 (2.1)	<.0001	191 (9.3)
Liver disease	19,310 (1.8)	<.0001	194 (4.8)	10,618 (2.0)	<.0001	94 (4.6)
Fluid/electrolyte disorders	13,979 (1.3)	<.0001	430 (10.6)	7,316 (1.4)	<.0001	205 (10.0)
Psychosis	13,474 (1.3)	<.0001	352 (8.7)	7,569 (1.4)	<.0001	163 (8.0)
Coagulopathy	12,663 (1.2)	<.0001	193 (4.8)	6,290 (1.2)	<.0001	91 (4.5)
Renal disease	12,558 (1.2)	<.0001	422 (10.4)	6,600 (1.2)	<.0001	204 (10.0)
Diabetes mellitus with complications	12,353 (1.2)	<.0001	485 (11.9)	6,193 (1.1)	<.0001	238 (11.6)
Valvular heart disease	10,449 (1.0)	<.0001	197 (4.9)	5,301 (1.0)	<.0001	100 (4.9)
Peptic ulcer disease without bleeding	7,570 (0.7)	<.0001	63 (1.6)	3,744 (0.7)	<.0001	47 (2.3)
Alcohol abuse	7,454 (0.7)	<.0001	138 (3.4)	3,521 (0.7)	<.0001	67 (3.3)
Paraplegia/hemiplegia	4,097 (0.4)	<.0001	81 (2.0)	1,955 (0.4)	<.0001	42 (2.1)

Note: CVD - collagen-vascular diseases
Note: See Appendix 1 for the technical definitions of these variables.

Table 3.2. Cont'd: Characteristics of the Individuals in the Datasets Used for CART Analysis
Values are counts (%) unless indicated otherwise

Variables	Training/Validation Data 2013/14-2014/15 # with outcome = 4,065 (0.38%)			Test Data 2015/16 # with outcome = 2,044 (0.38%)		
	No Outcome	p-value	With Outcome	No Outcome	p-value	With Outcome
Elixhauser comorbidities cont'd.						
Pulmonary circulatory disorders	4,039 (0.4)	<.0001	99 (2.4)	2,047 (0.4)	<.0001	45 (2.2)
Lymphoma	2,145 (0.2)	<.0001	57 (1.4)	1,156 (0.2)	<.0001	30 (1.5)
Hypertension with complications	1,759 (0.2)	<.0001	44 (1.1)	1,159 (0.2)	<.0001	21 (1.0)
Metastatic cancer	1,235 (0.1)	<.0001	105 (2.6)	721 (0.1)	<.0001	47 (2.3)
Weight loss	1,149 (0.1)	<.0001	52 (1.3)	596 (0.1)	<.0001	14 (0.7)
HIV/AIDS	809 (0.1)	0.0145	8 (0.2)	642 (0.1)	0.0375	6 (0.3)
Blood loss anemia	283 (0.0)	<.0001	15 (0.4)	121 (0.0)	<.0001	7 (0.3)
Dementia	15,968 (1.5)	<.0001	762 (18.8)	8,023 (1.5)	<.0001	348 (17.0)
Segal frailty score, terciles						
0.000-0.010	353,738 (33.4)	<.0001	186 (4.6)	181,028 (33.4)	<.0001	110 (5.4)
0.010-0.030	354,929 (33.5)		542 (13.3)	180,924 (33.4)		266 (13.0)
0.031-1.000	351,585 (33.2)		3,337 (82.1)	179,750 (33.2)		1,669 (81.6)
McIsaac frailty score						
0-3	341,885 (32.3)	<.0001	318 (7.8)	188,800 (34.9)	<.0001	202 (9.9)
3.5-5.5	373,570 (35.2)		625 (15.4)	183,124 (33.8)		340 (16.6)
6-23	344,797 (32.5)		3,122 (76.8)	169,778 (31.3)		1,503 (73.5)
ACG frailty flag	5,513 (0.5)	<.0001	335 (8.2)	2,642 (0.5)	<.0001	182 (8.9)
Timing of most recent ICU admission						
0-1 months	387 (0.0)	<.0001	12 (0.3)	189 (0.0)	<.0001	8 (0.4)
2-6	1,764 (0.2)		62 (1.5)	973 (0.2)		24 (1.2)
7-12	2,047 (0.2)		46 (82.0)	936 (0.2)		19 (0.9)
13-24	3,981 (0.4)		82 (2.0)	1,861 (0.3)		31 (1.5)
>24 or none	1,052,073 (99.2)		3,863 (95.0)	537,744 (99.3)		1,962 (96.0)

Note: ACG - Johns Hopkins Aggregated Clinical Groups™
Note: See Appendix 1 for the technical definitions of these variables.

Table 3.2. Cont'd: Characteristics of the Individuals in the Datasets Used for CART Analysis
Values are counts (%) unless indicated otherwise

Variables	Training/Validation Data 2013/14-2014/15 # with outcome = 4,065 (0.38%)			Test Data 2015/16 # with outcome = 2,044 (0.38%)		
	No Outcome	p-value	With Outcome	No Outcome	p-value	With Outcome
Timing of most recent cardiac catheterization						
0-1 months	591 (0.1)		14 (0.3)	307 (0.1)		8 (0.4)
2-6	2,912 (0.3)		53 (1.3)	1,471 (0.3)		21 (1.0)
7-12	3,363 (0.3)	<.0001	42 (1.0)	1,682 (0.3)	<.0001	25 (1.2)
13-24	6,430 (0.6)		63 (1.6)	3,053 (0.6)		29 (1.4)
>24 or none	1,046,956 (98.8)		3,893 (95.8)	535,190 (98.8)		1,961 (95.9)
Timing of most recent GI endoscopy						
0-1 months	5,296 (0.5)		50 (1.2)	3,108 (0.6)		25 (1.2)
2-6	25,280 (2.4)		177 (4.4)	12,932 (2.4)		86 (4.2)
7-12	27,951 (2.6)	<.0001	133 (3.3)	13,792 (2.6)	<.0001	71 (3.5)
13-24	49,853 (4.7)		232 (5.7)	25,307 (4.7)		126 (6.2)
>24 or none	951,872 (89.8)		3,473 (85.4)	486,564 (89.8)		1,736 (84.9)
Timing of most recent bronchoscopy						
0-1 months	64 (0.0)		s	52 (0.0)		0 (0.0)
2-6	392 (0.0)		17 (0.4)	178 (0.0)		7 (0.3)
7-12	438 (0.0)	<.0001	s	194 (0.0)	<.0001	6 (0.3)
13-24	811 (0.1)		16 (0.4)	374 (0.1)		6 (0.3)
>24 or none	1,058,547 (99.8)		4,021 (98.9)	540,905 (99.9)		2,025 (99.1)

Note: GI - gastrointestinal
Note: See Appendix 1 for the technical definitions of these variables.
†Timing backwards from the Evaluation Data: (A) 13-24 months prior, (B) 5-12 months prior, (C) 4-6 months prior, (D) 0-3 months prior

Table 3.2. Cont'd: Characteristics of the Individuals in the Datasets Used for CART Analysis
Values are counts (%) unless indicated otherwise

Variables	Training/Validation Data 2013/14-2014/15 # with outcome = 4,065 (0.38%)			Test Data 2015/16 # with outcome = 2,044 (0.38%)		
	No Outcome	p-value	With Outcome	No Outcome	p-value	With Outcome
Hospital days†						
(A) mean±SD	0.41 ± 3.67	<.0001	4.08 ± 12.80	0.36 ± 3.25	<.0001	3.48 ± 10.85
median (interquartile range; IQR)	0 (0, 0)	<.0001	0 (0, 0)	0 (0, 0)	<.0001	0 (0, 0)
(B) mean±SD	0.22 ± 2.44	<.0001	2.22 ± 8.69	0.20 ± 2.32	<.0001	2.20 ± 9.06
median (IQR)	0 (0, 0)	<.0001	0 (0, 0)	0 (0, 0)	<.0001	0 (0, 0)
(C) mean±SD	0.11 ± 1.61	<.0001	1.37 ± 6.41	0.11 ± 1.58	<.0001	1.52 ± 6.53
median (IQR)	0 (0, 0)	<.0001	0 (0, 0)	0 (0, 0)	<.0001	0 (0, 0)
(D) mean±SD	0.10 ± 1.38	<.0001	1.47 ± 5.87	0.10 ± 1.41	<.0001	1.77 ± 6.58
median (IQR)	0 (0, 0)	<.0001	0 (0, 0)	0 (0, 0)	<.0001	0 (0, 0)
Alternate Level of Care+Rehabilitation days†						
(A) mean±SD	0.17 ± 3.41	<.0001	2.55 ± 14.03	0.12 ± 2.71	<.0001	1.73 ± 12.22
median (IQR)	0 (0, 0)	<.0001	0 (0, 0)	0 (0, 0)	<.0001	0 (0, 0)
(B) mean±SD	0.08 ± 2.17	<.0001	1.17 ± 8.84	0.06 ± 1.76	<.0001	0.86 ± 6.86
median (IQR)	0 (0, 0)	<.0001	0 (0, 0)	0 (0, 0)	<.0001	0 (0, 0)
(C) mean±SD	0.05 ± 1.49	<.0001	0.70 ± 5.54	0.04 ± 1.43	<.0001	0.71 ± 5.77
median (IQR)	0 (0, 0)	<.0001	0 (0, 0)	0 (0, 0)	<.0001	0 (0, 0)
(D) mean±SD	0.04 ± 1.34	<.0001	0.63 ± 4.91	0.04 ± 1.28	<.0001	0.76 ± 5.65
median (IQR)	0 (0, 0)	<.0001	0 (0, 0)	0 (0, 0)	<.0001	0 (0, 0)

Note: SD - standard deviation
Note: See Appendix 1 for the technical definitions of these variables.
†Timing backwards from the Evaluation Data: (A) 13-24 months prior, (B) 5-12 months prior, (C) 4-6 months prior, (D) 0-3 months prior

Table 3.2. Cont'd: Characteristics of the Individuals in the Datasets Used for CART Analysis

Values are counts (%) unless indicated otherwise

Variables	Training/Validation Data 2013/14-2014/15 # with outcome = 4,065 (0.38%)			Test Data 2015/16 # with outcome = 2,044 (0.38%)		
	No Outcome	p-value	With Outcome	No Outcome	p-value	With Outcome
Outpatient clinic visits†						
(A) mean±SD	5.24 ± 5.47	<.0001	7.71 ± 7.26	5.37 ± 5.51	<.0001	8.16 ± 7.33
median (IQR)	4 (1, 7)	<.0001	6 (2, 11)	4 (1, 8)	<.0001	7 (3, 12)
(B) mean±SD	2.75 ± 3.11	<.0001	4.27 ± 4.39	2.82 ± 3.14	<.0001	4.41 ± 4.23
median (IQR)	2 (0, 4)	<.0001	3 (1, 6)	2 (0, 4)	<.0001	3 (1, 6)
(C) mean±SD	1.34 ± 1.71	<.0001	2.07 ± 2.37	1.37 ± 1.75	<.0001	2.09 ± 2.35
median (IQR)	1 (0, 2)	<.0001	1 (0, 3)	1 (0, 2)	<.0001	1 (0, 3)
(D) mean±SD	1.28 ± 1.69	<.0001	2.07 ± 2.44	1.32 ± 1.74	<.0001	2.12 ± 2.50
median (IQR)	1 (0, 2)	<.0001	1 (0, 3)	1 (0, 2)	<.0001	1 (0, 3)
Health Links – Info Santé days†						
(A) mean±SD	0.09 ± 0.97	<.0001	0.15 ± 1.20	0.09 ± 0.91	0.0017	0.15 ± 1.07
median (IQR)	0 (0, 0)	0.0001	0 (0, 0)	0 (0, 0)	0.0009	0 (0, 0)
(B) mean±SD	0.04 ± 0.51	<.0001	0.10 ± 0.85	0.04 ± 0.44	0.0888	0.06 ± 0.46
median (IQR)	0 (0, 0)	<.0001	0 (0, 0)	0 (0, 0)	0.0002	0 (0, 0)
(C) mean±SD	0.02 ± 0.28	<.0001	0.04 ± 0.35	0.02 ± 0.25	0.0011	0.04 ± 0.29
median (IQR)	0 (0, 0)	<.0001	0 (0, 0)	0 (0, 0)	<.0001	0 (0, 0)
(D) mean±SD	0.02 ± 0.25	<.0001	0.04 ± 0.37	0.02 ± 0.24	<.0001	0.04 ± 0.31
median (IQR)	0 (0, 0)	<.0001	0 (0, 0)	0 (0, 0)	<.0001	0 (0, 0)

Note: SD - standard deviation

Note: See Appendix 1 for the technical definitions of these variables.

†Timing backwards from the Evaluation Data: (A) 13-24 months prior, (B) 5-12 months prior, (C) 4-6 months prior, (D) 0-3 months prior

Table 3.2. Cont'd: Characteristics of the Individuals in the Datasets Used for CART Analysis
Values are counts (%) unless indicated otherwise

Variables	Training/Validation Data 2013/14-2014/15 # with outcome = 4,065 (0.38%)			Test Data 2015/16 # with outcome = 2,044 (0.38%)		
	No Outcome	p-value	With Outcome	No Outcome	p-value	With Outcome
Outpatient laboratory test counts†						
(A) mean±SD	4.73 ± 7.55	<.0001	7.10 ± 11.73	5.03 ± 7.88	<.0001	7.58 ± 11.77
median (IQR)	0 (0, 8)	0.0038	1 (0, 11)	0 (0, 8)	<.0001	2 (0, 12)
(B) mean±SD	2.54 ± 4.84	<.0001	3.96 ± 7.16	2.73 ± 5.07	<.0001	4.22 ± 7.39
median (IQR)	0 (0, 3)	<.0001	0 (0, 6)	0 (0, 4)	<.0001	0 (0, 6)
(C) mean±SD	1.23 ± 3.07	<.0001	1.90 ± 4.22	1.33 ± 3.25	<.0001	1.94 ± 4.08
median (IQR)	0 (0, 0)	<.0001	0 (0, 2)	0 (0, 0)	<.0001	0 (0, 2)
(D) mean±SD	1.24 ± 3.13	<.0001	2.08 ± 4.34	1.35 ± 3.33	<.0001	2.12 ± 4.47
median (IQR)	0 (0, 0)	<.0001	0 (0, 2)	0 (0, 0)	<.0001	0 (0, 2)
ATC4 prescription counts†						
(A) mean±SD	3.56 ± 3.75	<.0001	7.60 ± 5.42	3.55 ± 3.74	<.0001	7.45 ± 5.31
median (IQR)	3 (1, 5)	<.0001	7 (4, 11)	3 (1, 5)	<.0001	7 (3, 11)
(B) mean±SD	2.76 ± 3.15	<.0001	6.32 ± 4.65	2.79 ± 3.16	<.0001	6.27 ± 4.55
median (IQR)	2 (0, 4)	<.0001	6 (3, 9)	2 (0, 4)	<.0001	6 (3, 9)
(C) mean±SD	2.25 ± 2.80	<.0001	5.48 ± 4.19	2.29 ± 2.81	<.0001	5.45 ± 4.14
median (IQR)	1 (0, 3)	<.0001	5 (2, 8)	1 (0, 4)	<.0001	5 (2, 8)
(D) mean±SD	2.25 ± 2.85	<.0001	5.64 ± 4.31	2.30 ± 2.88	<.0001	5.71 ± 4.28
median (IQR)	1 (0, 3)	<.0001	5 (2, 8)	1 (0, 4)	<.0001	5 (2, 9)

Note: SD - standard deviation; ATC4 - fourth level of the Anatomic Therapeutic Chemical Classification system
Note: See Appendix 1 for the technical definitions of these variables.
†Timing backwards from the Evaluation Data: (A) 13-24 months prior, (B) 5-12 months prior, (C) 4-6 months prior, (D) 0-3 months prior

CART Results

The optimal tree had 21 levels of branching and a total of 2,644 terminal leaves (Appendix Table 2.1). The initial branch point was by residence in a PCH, immediately producing a terminal leaf containing all those in a PCH. In the training data, that leaf included all 5,954 individuals living in a PCH, of whom 470 (7.9%) experienced the outcome. Thus, the other leaves contained only those not living in a PCH.

An illustration of the way that CART can combine input variables in complex combinations is a terminal leaf with 14 individuals in the training data (11 in the validation data, and 8 in the test data). This subgroup comprised subjects who were:

- Female
- Living <105 km from Winnipeg or Brandon (whichever was closer)
- SEFI ≥ -0.65
- Two clinic visits in the 3 months prior to the Evaluation Date
- Hospital days were:
  - <25 in the most recent 3 months
  - <25 in the prior 7-12 months
  - ≥10 from 13-24 months prior
- ALC + rehabilitation days were:
  - <52 from 13-24 months prior
  - <42 from 7-12 months prior
- Outpatient laboratory tests were:
  - <14 outpatient laboratory tests performed in the most recent 3 months
  - <21 in the prior 7-12 months
- Prescriptions: 12-13 different chemical classes filled in the 4-6 months prior

The relative importance of the top 25 input variables, with the highest set arbitrarily at 1.0, is shown in Table 3.3 (see Appendix Table 2.2 for all 72 variables). A social determinant of health, socioeconomic status, had the highest importance in identifying the outcome, followed by living in a PCH. Living at home while awaiting a PCH bed (panelling) was much less important, being in 56th place with a relative importance of 0.05. Frailty scores occupied the 3rd and 5th variable importance slots; age was 6th; with those variables, the ACG frailty flag did not enter into the optimal tree at all. Utilization of outpatient care and drug prescriptions were the highest-ranked parameters of medical resource use, though generally the counts from the most remote portion of the 24-month lookback period were more influential. The first appearance of a count of hospital days was in the 14th slot, with importance less than half that of socioeconomic status. The 32 specified chronic diagnoses had relative importance values <0.29.

Table 3.3: Relative Importance of Top 25 Input Variables in the Optimal CART Tree Solution

Ranking	Input Variable	Relative Importance
1	Socioeconomic status (SEFI-2)	1.000
2	Lives in a personal care home	0.883
3	Segal frailty score	0.879
4	Distance from home to closest ICU	0.860
5	McIsaac frailty score	0.810
6	Age	0.756
7	Outpatient clinic visits: 7-12 months prior to Evaluation Date	0.587
8	Outpatient clinic visits: 13-24 months prior to Evaluation Date	0.580
9	Outpatient laboratory test counts: 13-24 months prior to Evaluation Date	0.577
10	ATC4 prescription counts: 7-12 months prior to Evaluation Date	0.558
11	ATC4 prescription counts: 4-6 months prior to Evaluation Date	0.549
12	ATC4 prescription counts: 13-24 months prior to Evaluation Date	0.535
13	ATC4 prescription counts: 0-3 months prior to Evaluation Date	0.504
14	Hospital days: 13-24 months prior to Evaluation Date	0.458
15	Outpatient laboratory test counts: 7-12 months prior to Evaluation Date	0.449
16	Outpatient clinic visits: 7-12 months prior to Evaluation Date	0.444
17	Outpatient clinic visits: 0-3 months prior to Evaluation Date	0.421
18	Outpatient laboratory test counts: 4-6 months prior to Evaluation Date	0.416
19	Hospital days: 0-3 months prior to Evaluation Date	0.401
20	Hospital days: 7-12 months prior to Evaluation Date	0.383
21	Hospital days: 4-6 months prior to Evaluation Date	0.301
22	Metastatic cancer	0.285
23	Outpatient laboratory test counts: 4-6 months prior to Evaluation Date	0.274
24	Statistical Area Classification	0.200
25	Open Home Care file	0.186

In the training data, the optimal tree performed well in identifying individuals with the outcome (Table 3.4); 493 individuals were contained in 41 terminal leaves each of which had ≥33% of its members experiencing the outcome. However, most of this performance towards our goal represented overfitting of the model to the training data, as this performance was not reproduced when applying the same terminal leaf definitions to the validation or test datasets (Tables 3.4 and 3.5). In the test data, these 41 leaves contained 429 individuals, but only 20 (4.7%) of them experienced the outcome. Expanding the range of terminal leaves in the training data to those with ≥20% or ≥10% outcomes likewise performed well in the training data, but this was not reproduced in the validation or test data.
Table 3.4: Performance of the Optimal Tree in Identifying Individuals with the Outcome

Table 3.4: Performance of the Optimal Tree in Identifying Individuals with the Outcome

	Outcome Percentages in Training Dataset								
	≥33% (41 Leaves)			≥20% (279 leaves)			≥10% (863 leaves)		
	Training Data	Validation Data	Test Data	Training Data	Validation Data	Test Data	Training Data	Validation Data	Test Data
# Subjects	493	376	429	3242	2291	2871	9849	6834	9111
# Outcomes	191	20	20	832	87	100	1632	144	171
% Outcomes	38.7	5.3	4.7	25.7	3.8	3.5	16.6	2.1	1.9
Lift*	102.0	14.0	12.3	67.5	10.0	9.2	43.6	5.5	4.9

* Lift measures performance of a tree at predicting events in a chosen subset of leaves, compared to the rate of events in the entire sample; for example, if the rate of events in the entire population is 1%, but in a given subset of leaves the rate is 20%, then the lift for this subset is 20.

Table 3.5: Reproducibility of Outcome Percentages Across Datasets from CART for Top Terminal Leaves in the Training Data

Training Data (%)	Validation Data (%)	Test Data (%)
47.1	11.8	0
46.7	5.0	20.0
45.5	14.3	16.7
45.5	0	0
45.5	25.0	0
45.5	10.0	0
41.7	0	0
41.7	0	12.5
41.7	8.3	10.0
41.7	0	0
40.0	0	0
40.0	0	14.3
40.0	50.0	0
40.0	0	0
40.0	0	0
40.0	14.3	0
40.0	20.0	0
40.0	0	0
40.0	0	28.6
40.0	0	0
40.0	0	0
40.0	10.0	0

Chapter 4:
Discussion and Implications

Main Finding

Although we leveraged the numerous variables and longitudinal nature of the data in the Manitoba Population Research Data Repository and the flexibility of CART analysis, we were not able to achieve the goal of prospectively identifying subgroups of community-dwelling Manitobans with a one in three chance of developing critical illness in the near future. This threshold was chosen as being "sufficiently high" to make it clinically useful, i.e., practical to design and test interventions targeted at these individuals and seeking to avoid, or substantially delay, the coming health event. Given the expected effort and costs that would be involved with such a population-based endeavour, practicality would likely also require identifying a sufficient absolute number of people who might benefit. We initially chose a "practicality threshold" of intervening on no more than three people to have a chance of avoiding one outcome of a critical illness event (≥33% of outcomes in high-risk leaves). And indeed, in the (overfitted) training dataset, this would be expected to translate to applying an intervention yearly to 411 people to address the heightened risk in 159 of them. If even half of those could have their critical illness or death avoided or delayed, approximately 80 lives might be saved yearly in Manitoba; such an effect would also be expected to improve the health and quality of life of these individuals, and conceivably also reduce overall health system costs. Said another way, in the training data, the people populating these subsets had a 102-fold higher rate of the outcome than the entire eligible population evaluated (lift).

Our hope was that this magnitude of benefit could be reproduced by applying the CART model to future data, but this was not the case. The proportion of individuals belonging to those subsets who had the outcome in the validation and test datasets was approximately 5% – indicating the need to apply an intervention to 20 people to even have a chance of avoiding one near-future critical illness. While this is substantially higher than our a priori estimate of the number needed to treat (NNT) of three, perspective on this figure is provided by comparison with other common medical interventions. It is not unusual for commonly used therapies to have NNT values larger than 20 (Table 4.1) [33]. Combining unit treatment costing with such NNT data allows us to estimate total costs for saving one life via routine outpatient interventions: $34,125 for treating hypertension with 20 mg/day of generic lisinopril (an intermediate dose of the most commonly prescribed agent) [34], and $65,700 for lung cancer screening with low dose thoracic CT scanning [35].

Table 4.1: Number Needed to Treat (NNT) for Various Therapeutic Interventions

Intervention	NNT for mortality	NNT (other outcome)
Outpatient Interventions		
Antihypertension treatment for 5-year adverse outcomes	125	67 (stroke)
Aspirin after acute ischemic stroke	79	140 (recurrent stroke)
Statin drugs for secondary prevention with known heart disease	83	30 (non-fatal heart attack)
Low dose CT scan for lung cancer screening in heavy smokers	219	
Antibiotics for exacerbation of Chronic Obstructive Pulmonary Disease	8	
Vitamin D for fracture prevention in elderly, institutionalized people		36 (hip fracture prevention)
Influenza vaccine		71 (preventing influenza)
Antibiotics for acute sinusitis		18 (symptomatic cure)
Inpatient Interventions		
Antibiotics for cirrhotics with upper gastrointestinal bleeding	22	4 (infection)
Thrombolysis for acute pulmonary embolism	34	
Thrombolysis for acute myocardial infarction	43	
Thrombolysis for acute ischemic stroke	10	
Early thrombectomy for large vessel ischemic stroke		2.6 (disability)
Early invasive therapy for unstable angina or acute myocardial infarction		62 (recurrent MI)
Defibrillation for cardiac arrest	2.5	
Hypothermia after cardiopulmonary resuscitation		6 (survival with good neurologic function)
Lung protective ventilation for Acute Respiratory Distress Syndrome	10	

Source: The NNT Group. Quick summaries of evidence-based medicine. https://www.thennt.com/home-nnt/

Though we lack data needed to estimate the average cost of some future dedicated intervention to identify, contact, clinically evaluate and treat conditions found to be the likely causes of near-future critical illness, we can make comparative estimates. Our CART analysis proved able to identify near-future critical illness at a 5% rate, i.e., 1 in 20 identified persons actually had the event in that near future. If we conservatively assumed that such an intervention could avoid the critical illness in 1 in 10 persons to whom it was applied, then the NNT is 200. Accordingly, to equal the cost per year of life saved for treating hypertension, such an intervention would need to cost <$170. While this figure is likely lower than a dedicated intervention for these individuals, it may well be compatible with an alternative approach of involving primary care providers in efforts to avoid near-future critical illness. One could imagine a relatively inexpensive automated infrastructure that alerts primary care providers about the need to assess individuals on their patient rosters who have a 1 in 20 chance of developing critical illness in the next 30-180 days.

Methodologic Issues

Our methodology had two salient strengths. We included a large number of input variables into the analysis, representing a wide variety of concepts known to relate to health and health care. A novel aspect was including longitudinal data on prior medical resource use, which we hypothesized would add considerably to the predictive ability of our analysis. The use of CART analysis was also a strength. Unlike regression modeling approaches most often used in analyses of medical data, CART is more powerful at identifying and easier to interpret with respect to complex interactions among covariates. Identifying multiple small subsets of subjects is difficult via regression but is a prominent strength of CART.

Unlike in many business applications of CART [36], further pruning of the tree (removing individual leaves from the end, back towards the origin) would not serve our purpose. Pruning a terminal leaf that fails to reproduce in an independent dataset would be expected to improve reproducibility, but as a result, the previous node (that had been split to generate the now-pruned terminal leaf) would now be a terminal leaf with a lower fraction of the outcome. This clearly does not advance our purpose.

Our choice of 30-180 days forward from the Evaluation Date as constituting the "near future" was chosen a priori from first principles but could be questioned. Extending the upper limit to one year or more would increase the number and overall population fraction of the outcome. Though we expected that it would be harder to identify persons at high risk as more time elapsed from the Evaluation Date, it is plausible that the correspondingly higher population risk might counteract that effect. Indeed, taking it to the extreme, if one sought to identify those at high risk into the far future, the population risk itself would become very high. However, doing so would lose the need for acting quickly to intervene, and would again become impractical as an actual public health intervention. It might be reasonable to repeat our analysis with the definition of "near future" changed to extend longer (e.g., 30-365 days), or shorter (e.g., 30-90 days). Furthermore, while our rationale for starting this interval at 30 days is clear, we would not expect a large number increment in outcomes from 0-30 days after the Evaluation Date, it is true that prior attempts at future prediction have not omitted this very early interval. Thus, as a sensitivity analysis it would be reasonable for future work to repeat our analysis using a 0-180 day interval.

The composite outcome chosen could also be questioned. Fundamentally, we sought to identify critical illness that could conceivably be anticipated and, if subject to timely intervention, delayed or avoided. We believe that non-elective ICU admissions that included use of artificial life support, excluding trauma or injury meet those criteria. The concept that non-palliative deaths should likewise be included requires explanation. It derives from the idea that any death is associated with critical illness, even if it did not lead to ICU admission, and even if it was brief (as in a cardiac arrest); this is based on the fact that – excluding death from external causes such as trauma, injury, and poisoning – all deaths result from failure of vital organs. The exclusion of palliative deaths recognizes that for some people in some circumstances, death cannot be avoided, and the goal is not to artificially prolong the dying process. A limitation of this concept is that there are many individuals who do not have a formal identification of palliative care, but nonetheless do not desire (or receive) aggressive medical interventions, such as ICU admission, when they become critically ill. For example, this is true of many residents of PCHs in Manitoba, who have a standing order of 'Do Not Resuscitate' but are not enrolled in any formal palliative care program. Ideally it would be possible to identify these individuals and, as was done with those enrolled in formal palliative care programs, exclude them from our cohort. But as this was not possible, their inclusion likely introduced misclassification in our outcome, potentially reducing the performance of our predictive model.

Regarding this issue, it is relevant that the initial branch point of the optimal tree was living versus not living in a PCH, and that those living in a PCH branched no further. This node was further subdivided in the maximal tree created from using only the training data; indeed, its ramification led to 27 terminal leaves with outcome fractions in the training data from 0-90% (data not shown). However, using the validation data to identify the optimal tree (i.e., the one with the highest worth), all 27 of these leaves were pruned, indicating that they did not reproduce in independent data; this could be consistent with many deaths in PCHs among persons who by virtue of not being enrolled in an official palliative care program are included in our outcome, but functionally were "palliative" in that they did not desire or receive aggressive medical interventions around their deaths. Those deaths may conceivably have very different predictors compared to those without such limitations on care and confound the ability of CART to reproducibly identify them. Notably, as all PCH residents were split off from the rest at the first branch point, excluding them to perform a sensitivity analysis would not change the results for the non-PCH residents.

Finally, our choice of using CART analysis to identify community-dwelling individuals with a high probability of near-future critical illness was not the only type of analysis that could have been used. In the area of data mining, there are numerous alternative methods that could be applied to our data, and which might possibly perform better than CART. These include latent class analysis, multiple channel latent class analysis, kernel nearest neighbor algorithm, dynamic topic modeling, ensemble time series clustering, and others. Future work in this area could investigate those alternative analytic options.

Variable Importance in Prediction

The predictive importance of frailty was notable. Frailty is a construct that is distinct from (but associated with) age, comorbidity and social determinants of health. It may be defined as a "syndrome of age-related physiological decline, characterized by marked vulnerability to adverse health outcomes" [37]. It is possible to be frail without being elderly. It is also possible to be frail without any specific, identified comorbid conditions. Frailty is associated with mortality and morbidity, and with an inability to benefit from aggressive medical interventions. Although the two original formulations of frailty require clinical evaluation [38], recent work has used administrative data to identify frail individuals [39–43]. In our CART analysis, both Segal's [39] and McIsaac's [40] administrative data definitions of frailty were among the five most influential input variables. That both were highly influential indicates some difference in the underlying constructs they represent. Moreover, that both frailty measures had relative importance almost three-fold higher than even the most influential specific chronic condition (metastatic cancer) is consistent with much of the influence of chronic conditions on future outcome being mediated by the frailty they cause, rather than the condition per se.

Although the longitudinal measures of medical resource use were prominent among the influential input variables for predicting the outcome, it was interesting that it was generally not their most recent values that were most important. Indeed, six measures of resource utilization from 4-24 months prior to the Evaluation Date were more influential than the first measure of utilization 0-3 months prior (ATC4 prescription counts, Table 3.3), which appeared as the 13th most important measure. This observation may indicate that our outcome relates more to longer-term processes than recent/sudden changes, and it may, in part, explain the poor performance of attempts to predict future clinical outcomes based on recent data [17–19].

Future Directions

Main Considerations

It appears that high fidelity prediction of near-future critical illness among community-dwelling adults is not possible with the types of input variables we used, and if possible at all will require including additional parameters. There are other variables available in the Repository that we did not include in our analysis, including immunizations, immigrant status, education data, justice data, emergency department visits, radiology test counts, and others. Perhaps a different way of incorporating the longitudinal data into the analysis would improve prediction. While it is not impossible that these strategies might dramatically improve predictive power and reproducibility, we believe it to be unlikely. Instead, we hypothesize that completely divergent variables, not generally available in administrative data for entire populations, will be necessary. These include innate biology, health behaviours, environmental exposures and other socioeconomic factors, further discussed in the Additional Variables section.

Finally, we believe our work allows for two main inferences. First is that to achieve prediction of future critical illness of very high fidelity, such as a NNT of 3, it is necessary to develop a stronger conceptual framework for identifying the full range of variables that might be influential, and to determine how they may be routinely captured at the population level. Second is that even with the predictive ability of the optimal predictive model identified in this work, further study is warranted to assess whether alerting primary care providers to the high-risk patients on their rosters could reduce the rate of near-future critical illness in those persons.

Additional Variables

Genetic polymorphisms are associated with specific serious disorders [44,45], death from specific disorders [46], as well as infections and death from infections, including sepsis [47–49]. Sepsis is a particularly important aspect of infection and critical illness; a syndrome marked by acute organ dysfunction due to infection [50]morphology, cell biology, biochemistry, immunology, and circulation, it is one of the most common causes of critical illness [51].

Epigenetic characteristics are associated with all-cause mortality, longevity and age-related diseases [52,53]. Furthermore, epigenetic influences on mortality may interact with other exposures, such as Vitamin D levels [54], which are also related to genetics [55], low socioeconomic status [56], chronic diseases [57], and susceptibility to infections [58,59].

Beyond the association of cigarette smoking with a variety of common causes of death, other health behaviours and obesity are influential. The risk of sepsis has been associated with diet [60,61]. Obesity is related to a number of chronic conditions and independently with premature death [62]; indeed, body mass index has a complex U-shaped relationship with mortality [63,64]. Even the physical environment in which people live (the "built environment") has been associated with some causes of death [65].

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Appendix 1: Life-Supporting Medical Therapies

Administrative Data Definitions

Appendix Table 1.1: Administrative Data Definitions of Life-Supporting Medical Therapies*

Life Support Modality	Definitions
Invasive mechanical ventilation	(1) Procedure codes for positive pressure ventilation via endotracheal tube or tracheotomy: 1.GZ.31.CA-ND, 1.GZ.31.CR-ND ** (2) Definition 1 OR procedure codes for intubation (1.FA.53.xx) OR tracheotomy (1.GJ.77.xx)
Intravenous vasoactive drugs	(1) Procedure code for use of any: epinephrine, dopamine, dobutamine, amrinone or isoproterenol: 1.ZZ.35.xx-E3 (2) Definition 1 OR diagnosis codes for shock or hypotension (E86, I95.8, R57.0, R57.1, R57.2, R57.9, R58, T78.2, T81.1)
Renal replacement therapy	(1) Procedure codes for hemodialysis, intermittent or continuous: 1.PZ.21.HQ-BR, 1.PZ.21.HQ-BS (2) Definition 1 OR procedure codes for hemodialysis catheter insertion (1.JQ.53xx, 1.JT.53xx, 1.KR.53.xx) (3) Definition 2 OR ICD-10-CA diagnosis codes for acute renal failure (N17.x, O08.4, O90.4, T79.5)

*Source: Canadian Discharge Abstract Database

**1.GZ.31 codes for mechanical ventilation are accompanied by an extent code for ≥96 hrs vs. <96 hrs, which became mandatory in fiscal year 2003. For the current study we considered a person as having received invasive mechanical ventilation if it was for any duration.

(1) - primary administrative data definition; (2) and (3) - secondary administrative data definitions

Contingency Tables

Appendix Table 1.2: Identifying Invasive Mechanical Ventilation via Procedure Codes for IMV in Hospital Abstracts for the Entire Cohort

		Reference Standard Identification		
		No	Yes	Total
Hospital Abstract Identification	No	9,303	926	10,229
	Yes	547	9,988	10,535
	Total	9,850	10,914	20,764

Appendix Table 1.3: Identifying Invasive Mechanical Ventilation via Procedure Codes for IMV or Intubation or Tracheostomy in Hospital Abstracts for the Entire Cohort

		Reference Standard Identification		
		No	Yes	Total
Hospital Abstract Identification	No	9,300	904	10,204
	Yes	550	10,010	10,560
	Total	9,850	10,914	20,764

Appendix Table 1.4: Identifying Invasive Mechanical Ventilation via Procedure Codes for IMV in Hospital Abstracts, Excluding Cardiac Surgery Patients

		Reference Standard Identification		
		No	Yes	Total
Hospital Abstract Identification	No	7,418	750	8,168
	Yes	270	7,298	7,568
	Total	7,688	8,048	15,736

Appendix Table 1.5: Identifying Use of Intravenous Vasoactive Agents via Procedure Code for Such Agents in Hospital Abstracts for the Entire Cohort

		Reference Standard Identification		
		No	Yes	Total
Hospital Abstract Identification	No	11,040	9,724	20,764
	Yes	0	0	0
	Total	11,040	9,724	20,764

Appendix Table 1.6: Identifying Use of Intravenous Vasoactive Agents via Procedure Code for Such Agents or Diagnosis Codes for Shock in Hospital Abstracts, for the Entire Cohort

		Reference Standard Identification		
		No	Yes	Total
Hospital Abstract Identification	No	10,661	7,456	18,117
	Yes	379	2,268	2,647
	Total	11,040	9,724	20,764

Appendix Table 1.7: Identifying Invasive Renal Replacement Therapy via Procedure Codes for Hemodialysis in Hospital Abstracts for The Entire Cohort

		Reference Standard Identification		
		No	Yes	Total
Hospital Abstract Identification	No	19,183	71	19,254
	Yes	674	836	1,510
	Total	19,857	907	20,764

Appendix Table 1.8: Identifying Invasive Renal Replacement Therapy via Procedure Codes for Hemodialysis or Hemodialysis Catheter Insertion in Hospital Abstracts for the Entire Cohort

		Reference Standard Identification		
		No	Yes	Total
Hospital Abstract Identification	No	19,110	70	19,180
	Yes	747	837	1,584
	Total	19,857	907	20,764

Appendix Table 1.9: Identifying Invasive Renal Replacement Therapy via Procedure Codes for Hemodialysis or Hemodialysis Catheter Insertion, or via Diagnosis Codes for Acute Renal Failure in Hospital Abstracts for the Entire Cohort

		Reference Standard Identification		
		No	Yes	Total
Hospital Abstract Identification	No	17,208	50	17,258
	Yes	2,649	857	3,506
	Total	19,857	907	20,764

Appendix Table 1.10: Identifying Invasive Renal Replacement Therapy via Procedure Codes for Hemodialysis in Hospital Abstracts, Excluding Chronic Dialysis Patients

		Reference Standard Identification		
		No	Yes	Total
Hospital Abstract Identification	No	19,067	41	19,108
	Yes	558	538	1,096
	Total	19,625	579	20,204

Appendix Table 1.11: Identifying any of Invasive Mechanical Ventilation, Intravenous Vasoactive Agents, or Renal Replacement Therapy for the Entire Cohort

		Reference Standard Identification		
		No	Yes	Total
Hospital Abstract Identification	No	6,752	2,998	9,750
	Yes	379	10,635	11,014
	Total	7,131	13,633	20,764

Appendix 2: Classification and Regression Tree (CART)

Methodology

We used Classification and Regression Tree (CART) analysis to identify subgroups of community- dwelling adults who experienced high rates of near-future critical illness [31,32]. CART uses input variables to divide all members of a cohort into mutually exclusive subgroups, each defined by a given value/range/category of each input variable. The result is a "tree" where each "terminal leaf" is one such subgroup.

CART is an extremely flexible type of decision tree algorithm, that uses recursive partitioning, and can account for a very large number of independent variables, automatically allowing for arbitrarily complicated interactions among the them [31,32]. For a binary outcome such as ours, CART seeks a solution maximizing the overall "purity" of leaves, in the sense that leaves have as great a fraction of zeros or of ones as possible [32]; a variety of different measures can be used as the measure of purity. CART grows trees in single steps, working on an existing node and seeking a single variable (and its' splitting value) that improves the purity of the daughter nodes over the parent node that was split. Input variables may be split once, multiple times, or not at all. Conditions that terminate splitting are: perfect purity is achieved; the chosen maximum number of branches is reached; the chosen minimum leaf size is reached for each leaf; or the chosen threshold p-value for continued splitting is exceeded.

To create and identify the tree providing the best predictive capacity, CART uses two datasets, termed the training and validation datasets. CART generates the full, maximal tree from the former, then uses the latter to identify the optimal subtree. Identifying the single best subtree begins with the original (maximal) tree of M leaves generated from the training dataset alone. It uses both the training and validation datasets in the following steps, in which it: (i) removes individual leaves from the end back towards the origin ("pruning"), generating all subtrees of leaf number M-1, M-2, M-3, etc., and (ii) calculates, for every such subtree, the "worth" of the tree using one of a number of possible parameters (e.g., PROFIT, lift, others). Using that measure of worth, it chooses the subtree of the highest worth containing M, M-1, M-2, M-3, etc. leaves. Among this family of optimal subtrees of different size, it chooses as the final tree the one that has a higher worth than any smaller tree, but equal or higher worth than any larger tree.

We chose to use CART for two reasons. First, we expected that identifying a substantial number of individuals who will develop critical illness in the near future would require finding a large number of diverse subgroups (represented by terminal leaves) in which ≥33% experienced the outcome. Such subgroups would require applying an eventual intervention to no more than three people to have a chance to avert or delay one episode of critical illness. Second, we expected that the longitudinal health data contained in the Repository would be critical to our goal of predicting near future critical illness. Specifically, we hypothesized that there are temporal patterns of health care resource use that are associated with higher risk of the outcome. We chose a priori time interval of 24 months before an Evaluation Date, which we divided into four intervals: (A) months 1-12, (B) month 12-18, (C) months 19-21 and (D) months 22-24, which is the most recent three-month period. Within each interval, separately for each type of medical resource use, we included the number of uses during that interval (e.g., physician visits). The flexibility of CART allows it to include counts from different intervals to relate the outcome to temporal patterns of resource use.

To create the CART model, we combined the FY2013 and FY2014 cohorts, and then randomly subdivided them, 60:40, into training and validation cohorts. We then assessed how this model performed on the 2015 cohort (which served as the test cohort). CART settings in SAS Enterprise Miner were: (a) minimum leaf size = 10, (b) maximum levels = 30, (c) 2-way or 3-way branching allowed, (d) splitting criteria were GINI [31] along with a threshold p-value of 0.20 using both Bonferroni and depth adjustments, (d) tree worth assessed via the lift measure on the top 2% of ranked observations [32]. Lift measures performance of a tree at predicting events in a chosen subset of leaves, compared to the rate of events in the entire sample. For example, if the population rate of events is 1%, but in a given subset of leaves the rate is 20%, then the lift for this subset is 20. In SAS Enterprise Miner, one specifies the percentage of records in the validation dataset ranked in descending order of predicted event rates, in our case we chose the top 2%.

Technical Definitions of the 72 CART Analysis Input Variables

Age – adults between 40 and 89; 5-year groupings

Biologic sex – Male, female

Socioeconomic status - The SEFI-2 score [66]. This area-level measure is calculated using the national census. It is reported by postal code, incorporating average values of household income, unemployment rate, education level, and proportion of single-parent families.

Ever received income assistance – Receipt of income assistance anytime before the Evaluation Date

Statistical area classification type - Derived by Statistics Canada from postal codes and the national census, it roughly assesses population density; categorized into census metropolitan area (CMA), census agglomeration (CA), strong metropolitan influenced zone (MIZ), moderate MIZ, weak MIZ, and no MIZ.

MIZ communities lie outside CMAs and CAs and are classified according to the degree of influence CMAs or CAs may have on them [67].

Distance from residence to closest ICU - Measured distance to the closer of Winnipeg or Brandon using postal code coordinates

Having an open Home Care file on the Evaluation Date

Panelled for personal care home (PCH) placement - Living in the community and having been panelled for admission to a PCH within the past 1 year, but not yet living in one

Living in a PCH - Long-Term Care levels 1-4 only

Chronic, comorbid medical conditions - These 31 binary variables represented individual conditions per Elixhauser et al. [68] – derived from inpatient and outpatient data in the 24 months before the Evaluation Date, using codes per Quan et al. [30]10th Revision (ICD-10.

Dementia - derived from inpatient and outpatient data in the 24 months before the Evaluation Date, using codes per Quan et al. [30]10th Revision (ICD-10.

Frailty, as measured by Segal et al. [39] A claims-based measure that ranges from 0 to 1. Includes data from the 6 prior months, and incorporates age, sex, race (omitted here), 16 specific diagnostic conditions, the Charlson Comorbidity Index and whether or not the individual was hospitalized.

Frailty, as measured by McIsaac et al. [40]. A claims-based measure that ranges from 0 to 30. Includes data from the prior year, it includes 30 variables: quintiles of socioeconomic status (for which we used SEFI-2), being on home oxygen (available in the Manitoba Homecare database), a history of falls (identified by ICD-10 codes W00.x-W19.x in any inpatient, Emergency Department, or outpatient claim), being in long-term care or homecare, the anticholinergic risk score (derived from the DPIN database) [69], 11 specific diagnostic conditions, the Charlson Comorbidity Index, 7 flags from the ACG system, administrative definitions for five conditions (chronic obstructive pulmonary disease, diabetes mellitus, congestive heart failure, hypertension, and acute myocardial infarction), and the Hospital-patient One-year Mortality Risk (HOMR) score. In McIsaac's formulation the five administrative data definitions for chronic conditions were those from the Ontario Institute for Clinical Evaluative Sciences; we substituted parallel definitions available at MCHP. And as HOMR is a post-admission measure, while our subjects were community-living individuals, we omitted this component, leaving the range of scores as 0-29.

Frailty, as assessed by the Johns Hopkins Adjusted Clinical Group® (ACG®) Case-Mix System version 9 [70]. This is a single, binary indicator of whether the individual has a diagnosis falling within any 1 of 12 clusters that represent medical problems associated with frailty.

Timing of the most recent admission to an ICU - derived from the DAD [25]. Categorized as 0-1 month, 2-6 months, 7-12 months, 13-24 months, or >24 months/never

Timing of the most recent cardiac catheterization procedure - categorized as 0-1 month, 2-6 months, 7-12 months, 13-24 months, or >24 months/never. Derived from Manitoba physician tariff codes 2302, 2304, 2306, 2307, 2308, 2325, 2327, 2234, 2305, 6263, 6264, 6267, 6268, 6270, 6278, 6279, 6280.

Timing of the most recent upper or lower gastrointestinal endoscopy - categorized as 0-1 month, 2-6 months, 7-12 months, 13-24 months, or >24 months/never. Derived from Manitoba physician tariff codes 3055, 3063, 3057, 3065, 3121, 3122, 3123, 3190, 3192, 3095, 3092, 3505, 3506, 3498, 3185, 3186, 3187, 3189, 3188, 3196, 3311, 3313, 3315, 3317, 3319, 3320, 3323, 3324, 3312, 3000, 3002, 3004, 3010, 3012, 3013.

Timing of the most recent bronchoscopy - categorized as 0-1 month, 2-6 months, 7-12 months, 13-24 months, or >24 months/never. Derived from Manitoba physician tariff codes 2113, 2121, 2126, 2112, 2120, 2115, 2117, 2118.

Number of acute hospital days – measured during four intervals in 2 years before the Evaluation Date: (A) 13-24 months prior, (B) 7-12 months prior, (C) 4-6 months prior, and (D) 0-3 months prior. Days in scheduled/planned hospitalizations were excluded, as were days for: respite care, routine obstetrical hospitalizations (identified by the Most Responsible Hospital Diagnosis being delivery), days spent in Alternate Level of Care, and in rehabilitation facilities. Full or partial hospital days all counted as 'one' day. Obtained from the DAD.

Number of days spent either designated as being at an "Alternate Level of Care" (ALC) in a hospital, or in a rehabilitation facility – measured during four intervals in 2 years prior to the Evaluation Date: (A) 13-24 months prior, (B) 7-12 months prior, (C) 4-6 months prior and (D) 0-3 months prior. Typically, ALC days are used while awaiting transfer to a lower level of care, such as a nursing home [71]. Obtained from the Rehabilitation Database and the DAD.

Number of outpatient clinic visits – Included physician, nurse practitioner and primary care nurse visits during 4 intervals in 2 years prior to the Evaluation Date: (A) 13-24 months prior, (B) 5-12 months prior, (C) 4-6 months prior, and (D) 0-3 months prior. Includes both generalist and specialist practitioners. Excludes: outpatient surgeries; routine obstetrical visits (indicated by ICD-9 diagnosis codes of V22 or V23); visits to pediatricians, radiologists, pathologists, anaesthesiologists, emergency medicine physicians, optometrists, chiropractors, midwives; visits on the same day in which the individual was hospitalized. Obtained from Medical Services Data, tariffs with prefix of 7. Multiple tariffs submitted on the same date by the same practitioner were counted as a single visit.

Number of separate days during which the individual made one or more calls to Manitoba Health Links - Info Santé – measured during four intervals in 2 years prior to the Evaluation Date: (A) 13-24 months prior, (B) 7-12 months prior, (C) 4-6 months prior, and (D) 0-3 months prior. Health Links - Info Santé is a phone-based nursing triage system in Manitoba, available around-the-clock, where registered nurses follow assessment guidelines to triage health issues [72]. Obtained from the Health Links - Info Santé database.

Number of outpatient laboratory tests performed – measured during 4 intervals in 2 years before the Evaluation Date: (A) 13-24 months prior, (B) 5-12 months prior, (C) 4-6 months prior, and (D) 0-3 months prior. Groups of tests usually done together were counted as a single test (blood counts, lipids, basic serum electrolyte panel, extended serum electrolytes, urinary electrolytes, serum B12 and folate, liver panel, thyroid panel, coagulation panel, urinalysis, intradermal allergy panel, allergy patch test panel, portions of individual cultures with or without sensitivity testing). Excludes tests performed during Emergency Department visits and testing for pregnancy. Obtained from Medical Services Data, tariffs with prefix of 8.

Number of dispensed prescription medications – measured during four intervals in 2 years before the Evaluation Date: (A) 13-24 months prior, (B) 7-12 months prior, (C) 4-6 months prior and (D) 0-3 months prior. This was restricted to agents included in the provincial medication formulary (Manitoba Pharmacare). Agents were classified according to their chemical (ATC4 level) [73]. Two agents of the same chemical subgroup (e.g., angiotensin converting enzyme inhibitors) would be counted as one prescription, regardless of the number of refills in that period, or the number of pills dispensed. Also, multiple prescriptions for the same ATC4 level of agent filled in the same time interval counted as one prescription. Thus, this measure counts the number of different classes of prescription pharmaceuticals that were filled in the given time interval. Obtained from the Drug Prescription Information Network (DPIN) database

Appendix Table 2.1: Branching Results of the Optimal CART Tree Branching

Number of Branches	Number of Terminal Leaves	Percent of All Terminal Leaves
1	1	0.04
4	8	0.3
5	17	0.64
6	33	1.25
7	61	2.31
8	71	2.69
9	78	2.95
10	81	3.06
11	133	5.03
12	104	3.93
13	138	5.22
14	192	7.26
15	150	5.67
16	133	5.03
17	123	4.65
18	124	4.69
19	136	5.14
20	146	5.52
21	113	4.27
22	126	4.77
23	86	3.25
24	123	4.65
25	83	3.14
26	106	4.01
27	88	3.33
28	63	2.38
29	63	2.38
30	64	2.42
Total	**2644**	**99.98**

CART Input Variable Results

Appendix Table 2.2: Relative Importance of Input Variables in the Optimal CART Tree Solution

Ranking	Input Variable	Relative Importance
1	Socioeconomic status (SEFI-2)	1.000
2	Lives in a personal care home	0.883
3	Segal frailty score	0.879
4	Distance from home to closest ICU	0.860
5	McIsaac frailty score	0.810
6	Age	0.756
7	Outpatient clinic visits: 7-12 months prior to Evaluation Date	0.587
8	Outpatient clinic visits: 13-24 months prior to Evaluation Date	0.580
9	Outpatient laboratory test counts: 13-24 months prior to Evaluation Date	0.577
10	ATC4 prescription counts: 7-12 months prior to Evaluation Date	0.558
11	ATC4 prescription counts: 4-6 months prior to Evaluation Date	0.549
12	ATC4 prescription counts: 13-24 months prior to Evaluation Date	0.535
13	ATC4 prescription counts: 0-3 months prior to Evaluation Date	0.504
14	Hospital days: 13-24 months prior to Evaluation Date	0.458
15	Outpatient laboratory test counts: 7-12 months prior to Evaluation Date	0.449
16	Outpatient clinic visits: 7-12 months prior to Evaluation Date	0.444
17	Outpatient clinic visits: 0-3 months prior to Evaluation Date	0.421
18	Outpatient laboratory test counts: 4-6 months prior to Evaluation Date	0.416
19	Hospital days: 0-3 months prior to Evaluation Date	0.401
20	Hospital days: 7-12 months prior to Evaluation Date	0.383
21	Hospital days: 4-6 months prior to Evaluation Date	0.301
22	Metastatic cancer	0.285
23	Outpatient laboratory test counts: 4-6 months prior to Evaluation Date	0.274
24	Statistical Area Classification	0.200
25	Open Home Care file	0.186
26	Diabetes mellitus with complications	0.181
27	Health Links – Info Santé days: 7-12 months prior to Evaluation Date	0.178
28	Chronic pulmonary disorders	0.176
29	ALC+Rehabilitation days: 13-24 months prior to Evaluation Date	0.160
30	Sex	0.159
31	ALC+Rehabilitation days: 7-12 months prior to Evaluation Date	0.157
32	Timing of most recent ICU admission	0.150
33	Dementia	0.145
34	Cancer without metastases	0.144
35	Obesity	0.140
36	Congestive heart failure	0.135
37	Timing of most recent cardiac catheterization	0.134
38	Cardiac arrythmia	0.131
39	Timing of most recent GI endoscopy	0.126
40	Rheumatoid arthritis/collagen vascular disease	0.113

Appendix Table 2.2 Cont'd: Relative Importance of Input Variables in the Optimal CART Tree Solution

Ranking	Input Variable	Relative Importance
41	Renal disease	0.111
42	Ever received income assistance	0.109
43	Hypertension with complications	0.102
44	Other neurologic disorders	0.099
45	Valvular heart disease	0.097
46	Paraplegia/hemiplegia	0.096
47	Hypertension without complications	0.094
48	Drug abuse	0.094
49	Psychosis	0.093
50	Health Links – Info Santé days: 4-6 months prior to Evaluation Date	0.075
51	Weight loss	0.074
52	HIV/AIDS	0.074
53	Lymphoma	0.055
54	Alcohol abuse	0.054
55	Pulmonary circulation disorders	0.051
56	Paneled for long-term care	0.046
57	Peripheral vascular disease	0.046
58	Health Links – Info Santé days: 13-24 months prior to Evaluation Date	0.045
59	Depression	0.044
60	ALC+Rehabilitation days: 0-3 months prior to Evaluation Date	0.043
61	Coagulopathy	0.040
62	Health Links – Info Santé days: 0-3 months prior to Evaluation Date	0.037
63	Fluid/electrolyte disorders	0.035
64	Liver disease	0.032
65	Deficiency anemia	0.027
66	Peptic ulcer disease without bleeding	0.026
67	ALC+Rehabilitation days: 4-6 months prior to Evaluation Date	0.000
68	Blood loss anemia	0.000
69	Hypothyroidism	0.000
70	Timing of most recent bronchoscopy	0.000
71	Diabetes mellitus without complications	0.000
72	ACG frailty flag	0.000

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