Role of Multimorbidity and Patterns of Care in Patients with Acute and Chronic Conditions

by

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ABSTRACT

Evidence surrounding the role of multimorbidity in an acute care setting, as well as factors associated with improved health outcomes in this patient population, is significantly lacking. Therefore, the objectives of this program of research were to determine the role of multimorbidity on short term morbidity and mortality in patients managed for an acute event and to evaluate the relationship between continuity of care and multimorbidity on short term morbidity and mortality in patients at high risk of adverse outcomes. These objectives were achieved through two related studies. First, a prospective cohort study of 6000 patients with community- acquired pneumonia (CAP) was conducted to evaluate the impact of multimorbidity on 90-day death, hospital admission and emergency department (ED) visits. The results indicated that multimorbidity was common in a population of patients experiencing an acute event with one-third of all patients in our study having multimorbidity. Moreover, multimorbidity was independently associated with an increased risk of death, hospitalization, or return to ED within 90 days of discharge. Although multimorbidity is largely evaluated in patients with chronic conditions, the current research suggests that multimorbidity has a significant impact in acute conditions as well. Building upon these findings, the second study evaluated the potential role of continuity of care in mitigating the impact of multimorbidity in patients at high risk of adverse outcomes. Utilizing a retrospective cohort of almost 3000 patients with incident type 2 diabetes, a similar, independent association between better continuity of care and a lower risk of death or all-cause hospitalizations at 1 year, was observed for both patients with and without multimorbidity. Furthermore, similar to our previous study in acute care, multimorbidity

was also associated with significant increased risk of adverse outcomes. Collectively, this research suggests that clinicians and health care systems need to implement strategies to mitigate the negative impact of multimorbidity on patients. A potentially effective approach to achieve this is to improve follow-up and optimize continuity of care. Although this approach is likely reasonable for both acute and chronic disease settings, further research is required to affirm these findings in acute settings. Regardless, when managing or making site-of-care decisions for patients in acute or chronic settings, more attention should be paid to comorbidities and multimorbid conditions a patient may have.

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LIST OF ABBREVIATIONS

CAP- Community acquired pneumonia

ED- Emergency department

COPD- Chronic obstructive pulmonary disease

GERD- Gastroesophageal reflux disease

UPC- Usual Provider of Continuity

PSI- Pneumonia Severity Index

HF- Heart failure

CKD- Chronic kidney disease

ESRD- End stage renal disease

aPSI- Acute Pneumonia Severity Index

aHR- Adjusted hazard ratio

CI- Confidence interval

ICD-9-CM- International Classification of Diseases, Ninth Revision, Clinical Modification

ACG- Adjusted Clinical Groups

aOR- Adjusted odd's ratio

CHAPTER 1: INTRODUCTION

1.1 Statement of the Problem

1.1.1 Multimorbidity

Though the definition of chronic disease varies widely across the literature, it is generally known as a condition which has a duration of more than one year and results in functional limitation and the need for ongoing medical care.[1-4] The most common chronic conditions worldwide include heart disease, stroke, cancer, chronic respiratory disease and diabetes.[5] Over the last century, the major causes of death and disability have shifted from a predominance of nutritional deficiencies and infectious diseases to conditions classified as chronic. This shift has been termed "the epidemiologic transition".[6] Because people are living longer, they are more likely to experience chronic disease, as ageing is an important marker of the accumulation of modifiable risk factors for chronic disease. In Canada, 14% of the population is over 65 years and by 2036, this number is expected to increase to almost 25% or approximately 10 million people.[7] Furthermore, many acute events such as pneumonia, acute coronary syndrome and stroke were historically associated with high initial mortality, but through advances in medicine, are now survivable. These conditions, however, are still associated with significant downstream sequelae, which also contribute to the development of chronic disease.[8]

As chronic diseases share common risk factors, most people with chronic disease usually have more than one co-existing chronic condition and are influenced by a number of complex interactions..[9-11] Non-modifiable risk factors such as age, sex and genetics, as

well as modifiable risk factors including high blood pressure, elevated blood glucose, abnormal blood lipids, overweight/obesity and tobacco use all contribute to the development of chronic disease.[12] These risk factors tend to cluster within individuals, which can lead to the development to multiple chronic diseases.

The presence of more than one chronic disease within an individual has been referred to as multimorbidity, although the definition of multimorbidity varies widely across the literature. These discrepancies in terminology stem from differences in opinion as to what is considered multimorbidity as opposed to a comorbidity. While some consider the terms synonymous, others do not; there is little to no consensus on the subject. [9, 13, 14] The simplest definition of comorbidity is the presence of more than one distinct condition in an individual.[15] Some have argued, however, that the definition of comorbidity should in fact consider the nature of the health conditions, the relative importance of the co-occurring conditions, the chronology of presentation of the conditions and expanded conceptualizations.[13] Others have argued that the definition of comorbidity depends on the context of the research question (i.e., clinical care, epidemiology or health services planning and financing).[13] Overall, comorbidity is most often defined in relation to a specific index condition. The question of which condition should be designated the index condition is not self-evident, therefore, multimorbidity has been increasingly used to refer to the co-occurrence of multiple chronic or acute diseases and medical conditions within one person without any reference to an index condition.[9] This definition is also not agreeable to all. Generally, multimorbidity is defined based on an individual having a host of co-existing health conditions, however, some suggest that only chronic conditions

be considered in this definition rather than including chronic, acute and other medical conditions.[14] If one agrees upon the "chronic disease" definition of multimorbidity, the concept is further complicated by the choice of which chronic conditions to include when measuring multimorbidity. While some studies of multimorbidity consider diseases such as arthritis, psoriasis, migraines and chronic sinusitis in their definition,[16] others do not.[17] To complicate matters even further, it has also been suggested that measures of multimorbidity should not only evaluate the numbers of co-existing conditions an individual may have, rather, a summary index should be calculated based on the number of conditions as well as the severity of the conditions.[18] Creating weighted multimorbidity measures can be useful when determining its impact on a future outcome, however, the weighted measure is likely only useful for the specific outcome it was developed for.[9] Moreover, using a weighted measure is often not practical in the clinical decision-making process; thus, clinicians tend to focus on a specific disease state or a general count of disease conditions in formulating decisions.

In short, the definition of multimorbidity is complex and researchers are currently working towards a more uniform methodology. For our purposes, we considered multimorbidity to be the existence of two or more chronic conditions within an individual. This definition was chosen as it best fits the context of our research question and is one of the most commonly used definitions across the literature.[16, 19, 20 , 21 , 22-28] Moreover, the chronic conditions chosen as part of our definition have been well validated to predict poor health outcomes.[29, 30]

Irrespective of its definition, multimorbidity indicates clinical complexity and significant disease burden for individual patients. Because of this, there is an increasing movement by both the medical and research communities to lessen the emphasis placed on the treatment and study of discrete disease states and rather to focus on the whole patient that can often have multiple coexisting conditions.[31-34] This paradigm shift is crucial given that multimorbidity has become the norm in modern society.[35, 36] Although marked variations exist among studies of the prevalence of multimorbidity, it is generally considered to be common. A systematic review found that estimates range from 30% to approximately 90% in those over the age of 65, while multimorbidity remains highly prevalent in those under the age of 65 as well (estimates range from 10% to 50%).[37] These variations tend to exist due to differences in the setting under study (primary care setting vs general population) and the methodology used (operational definition of multimorbidity, number of diagnoses considered). In Canada, over 46% of those 65 and over are considered to have multimorbidity,[16, 37] with 17% of individuals under the age of 35 also living with multimorbidity.[23]

In addition to age, there are other important predictors and correlates of multimorbidity which have been explored in the literature. Socioeconomic factors are posited to have an impact on the development of multimorbidity through a number of mechanisms including smoking,[38] diet,[39] alcohol consumption, and physical activity,[40] as well as living conditions, chronic stress and access to the healthcare system. Overall, the literature has found an inverse relationship between low socioeconomic status and multimorbidity. Low levels of education, income and occupational based socioeconomic status have been

associated with increasing levels of co-existing chronic conditions.[14, 16, 23, 41-47] Low self-perceived social standing as well as not belonging to a social network have also been found to be important factors behind the development of multimorbidity.[45, 46] No association between literacy and multimorbidity, however, has been established in the literature. [28]

Considering the large number of risk factors, predictors and correlates of multimorbidity, it is not surprising that patients with multimorbidity can experience a range of disorders. Although most researchers agree that multimorbidity is diverse, identifying patterns amongst this diversity is important to inform policy as well as clinical practice. Individuals can experience both concordant conditions and discordant health problems, adding to the clinical complexity of this high-risk population.[32] Concordant conditions represent part of the same overall risk profile for the index condition under study and have common pathophysiological mechanisms that underlie disease aggregation, while discordant health problems are not directly related in pathogenesis or predisposing risk factors. In patients with diabetes, for example, hypertension, dyslipidemia, and ischemic heart disease are considered concordant conditions, while chronic obstructive pulmonary disease (COPD) and chronic pain are considered discordant. This being said, it is unlikely that any given chronic conditions within the same individual would be considered completely unrelated. Given the high prevalence of obesity and physical inactivity in the population, it is not surprising that conditions related to these factors represent some of the most common combinations of chronic disease clusters.[48] A typical pattern of chronic disease described in the literature is that of the "metabolic

syndrome" which is composed of hyperlipidemia, hypertension, heart disease and obesity.[23, 49] Other combinations of conditions include mental health disorders with thyroid disease and chronic pain as well as COPD and GERD.[50-55] Although these specific patterns have been established, it is important to realize that these associations may not follow previous biomedical research,[56] and some studies even suggest that medication use and socioeconomic status could be risk factors in the aggregation of certain diseases.[57]

1.1.2 Multimorbidity in acute care

Patients with multiple chronic conditions are likely to require repeated admissions to hospital for acute or episodic care that is imposed upon the needs of their chronic conditions.[58-62] Studies have found that acute exacerbations or complications of chronic disease account for approximately 60% of hospital admissions in those with pre-existing chronic disease, and that acute illness unrelated to comorbidity is responsible for the remaining hospital admissions.[63] While comorbidity can influence many different outcomes of hospital care such as length of stay,[64-66] the development of complications,[65-70] and surgical outcomes,[64, 71] the cumulative effect of multimorbidity on risk after the acute event has not been well studied. Research that has been conducted in this subject area is scarce, involves a diverse group of acute conditions, and has produced conflicting results. For example, in a general population admitted to hospital for any acute condition, those with the greatest levels of comorbidity were the most likely to be re-admitted to hospital both at 30-days and 1-year.[72] In terms of disease-specific studies, obese individuals were 2.1 times more likely than normal weight individuals to be hospitalized

for influenza compared to normal weight individuals,[73] and comorbid conditions were associated with early death in those hospitalized for acute pancreatitis.[74] However, in patients who were hospitalized with community- acquired pneumonia (CAP), COPD patients had no significant differences in their 30-day mortality compared with non-COPD patients.[75] It is therefore apparent that there is a paucity of evidence around this research question. Thus, the extent to which multimorbidity influences the risk of adverse events post-discharge for an acute event requires further study, given that the presence of multimorbidity is hypothesized to provide important prognostic information for the post-discharge period and can also influence decisions around time of discharge and triage.

1.1.3 Impact of multimorbidity in chronic care

Because multimorbidity has become so common in the general population there is great interest in its effects on health outcomes outside of the acute care setting. First, a number of studies have evaluated the effects of multimorbidity on mortality. Although the definition of multimorbidity varies from study to study, as do the populations of interest, the vast majority of studies have found clinically important increases in risk of death in those with multimorbidity compared to those without multimorbidity. Relative measures indicate the magnitude of this effect ranges from a 7% increased risk to an 82% increased risk.[26, 76-79] However, the association between multimorbidity and mortality in older ages remains controversial.[80-83]

There is also evidence to suggest that the existence of multiple chronic conditions within an individual is associated with significant increases in healthcare utilization. Indeed, those with multimorbidity have been found to be at an increased risk of all-cause hospital admission,[77, 78, 84, 85] as well as cause-specific hospital admission (including cardiovascular, heart failure related and ambulatory care sensitive hospital admission),[77, 78, 86] and emergency department visits.[25] An overall increase in physician visits has also been observed with multimorbidity, especially to specialist care providers.[87]

Multimorbidity is associated with decreases in other health indicators including clinically important reductions in health related quality of life.[24, 88] All studies included in a recent systematic review came to this same general conclusion; however, they also found this relationship may be affected by a patient's age or gender.[88] Not surprisingly, multimorbidity was found to mostly effect physical dimensions of health related quality of life,[89-91] however, data from one study suggested that social and psychological dimensions may be affected in patients with 4 or more diagnoses.[92] Other studies have also suggested that multimorbidity may be associated with depression and distress.[14] Similarly, numerous studies have found a direct relationship between the number of chronic conditions an individual has and risk of disability (mobility loss and loss of functional independence).[43, 59, 86, 88, 93-99] This relationship is relatively consistent across the literature, considering only one study in a recent systematic review did not find an association.[14]

In addition to the humanistic impacts of multimorbidity, it is also important to note its substantial burden on the healthcare system in terms of cost. The number of chronic conditions an individual has is significantly associated with the number of prescriptions, referrals and expenditures they may incur.[84, 86, 100-104] Moreover, it has been shown that the per capita expenditures for Medicare patients tends to increase along with the number of co-existing chronic conditions: from $211 among beneficiaries without a chronic condition to $13,973 among beneficiaries with 4 or more chronic conditions.[105] Additionally, patients with more than one chronic condition are estimated to account for 95% of all Medicare spending.[3]

1.1.4 Mitigating factors to improve outcomes in multimorbidity

Multimorbidity poses challenges for research due to its inherent complexity.[106, 107] Little attention has been given to the difficulties of managing multiple and potentially conflicting illnesses in acute care, despite the fact most believe these patients are at significant risk of downstream adverse outcomes. Not surprisingly, the complexity of care required for these patients when they are admitted to hospital or the emergency department is substantial as a result of these comorbid conditions. For instance, it is hypothesized that these patients are not receiving the appropriate care they require given that current healthcare systems are organized historically to respond rapidly and efficiently to any acute illness or injury that comes through the door, not the management of chronic disease.[108,109] For example, it has been found that patients with comorbidities perceived that acute care services did not fully acknowledge or accommodate the comprehensive care they required,[108] and also highlighted the need for comprehensive

discharge planning.[110] Once a person with acute disease and multimorbidity is discharged from hospital, little is known in regard to the impact that multimorbidity has on their progress and outcomes, let along factors which could improve these health outcomes.[111] The acute care setting could therefore provide the opportunity for health care professionals to link resources and oversee the care and management of comorbidities, to enable patients to return home with an enhanced health status that can be maintained.[108] Specifically, when a person with a variety of chronic conditions is admitted to acute care, the continuity and coordination of care for patients should be emphasized in order to support this potential improvement in health status. Thus, there is a clear need for research that informs health care professionals on the impact comorbidities can have in people experiencing an episodic illness event. More specifically, a greater understanding of how multimorbidity impacts downstream health outcomes in patients with acute conditions is urgently needed. Without a better understanding of the role of multimorbidity in the acute care setting, the implementation and evaluation of strategies to reduce its impact will be difficult.

To date, most of our evidence on how best to manage multimorbidity has been generated from the non-acute care setting. Despite the fact that evidence based clinical practice guidelines exist for many chronic conditions, most still focus on discrete disease states and only make recommendations for one or two conditions at a time.[112-114] Moreover, although there have been a number of studies on the effects of primary care interventions to manage those with multimorbidity, results have been mixed. A systematic review by Smith and colleagues found a trend towards improved blood pressure, prescribing and

drug adherence in most of their included studies.[115-117] Overall, however, they acknowledge that it appears difficult to improve other health outcomes such as hospital admission in this particular population.[117-122] They also hypothesize that interventions focusing on specific combinations of common conditions, particular risk factors in comorbid conditions or functional difficulties in multimorbidity, may be more effective for improving health outcomes.[116] Additionally, a number of studies have evaluated factors such as quality of care as well as receipt of preventative care services in patients with multimorbidity, however, none of these studies evaluated the impact of these factors on health outcomes.[116]

One area that is garnering increasing attention is related to the concept of continuity of care. Some have argued that it is not multimorbidity per se that is associated with increasing downstream adverse events, rather, it is the fact that these patients are receiving fragmented care as a result of their multimorbidity. Thus, many postulate that continuity of care may be key to improving care in chronic disease populations at high risk of multimorbidity. Continuity of care likely also plays a substantial role in improving care in acute disease populations, however, the unplanned nature of acute events makes the evaluation of continuity of care difficult.

Although the concept of continuity is not new to the literature, its definition has shown great overlap with related concepts (such as coordination or quality of care) and the differences between these concepts are often unclear.[102, 123, 124] Some definitions of

continuity of care refer to it as the process by which a patient and physician are cooperatively involved in ongoing health care management with the goal of high-quality, cost effective medical care.[125] In other words, continuity of care characterizes the relationship between individual patients and their physicians over time.[126] A different view of continuity has been proposed, stating that those responsible for the care of patients with prolonged illness and complex needs must be met by professionals with a range of skills across a number of settings. Put simply, this definition refers to the extent to which services are received as part of a coordinated and uninterrupted succession of events consistent with the medical needs of patients.[127] Thus, two core concepts of continuity emerge: one is related to continuity of care as a continuous caring relationship between a physician and a patient (also known as personal continuity) and the latter refers to continuity as seamless service between different healthcare professionals and settings.

A number of methods to describe continuity of care have been developed based on both objective and subjective measures.[126] Objective measures are usually calculated as indices, an example of which includes the Bice-Boxerman continuity of care index. This measure reflects the relative share of all of a patient's visits during the year that they are billed by distinct providers and or practices.[125] Other objective measures of continuity of care include indices related to duration,[128, 129] dispersion,[130, 131] and sequence of physician visits.[132-135] Subjective measures of continuity of care are usually based on instruments or questionnaires administered to patients.[132, 136] Examples of these instruments include the Components of Primary Care Index which measures personal continuity, team continuity and cross boundary continuity from the patient perspective based on a 19 item

questionnaire,[125] as well as the Patient Continuity of Care Questionnaire, which is a 27 item instrument used to measure patient perceptions of factors impacting continuity of care following discharge from hospital.[137]

Although both objective and subjective measures of continuity have been proposed, there is a level of concordance between these measures. One study found that high levels of continuity for patients (as calculated through an objective measure using administrative health data) was associated with longer patient-provider relationships, greater patient-perceived provider knowledge of the patient's medical condition and history and more confidence in the provider, as measured through subjective instruments administered to patients.[138] For our purposes, we will utilize a density index called Breslau's Usual Provider of Continuity or UPC to define continuity of care.[139] This index is one of the most commonly used measures in the literature,[140] and is calculated as the number of physician visits to the predominant physician divided by the total number of physician visits. Score can range from 0 (perfect "discontinuity") to 1 (perfect continuity).[141-143]

Keeping in mind the different perspectives from which to view continuity of care, a number of studies have found that it can lead to improvements in a number of health indicators. As many as four systematic reviews have been conducted that suggest continuity of care decreases the risk of morbidity and mortality in a range of populations,[142, 144 ,145, 146] however, this relationship varies according to the health outcome and population under study, as well as the measure of continuity used. Some

studies suggest that reductions in emergency department utilization ranged from 25%-35% with continuity of care,[142, 144, 145] as did 2%-30% reductions in hospital admission.[135, 147,148] Continuity of care is also associated with a nearly 50% reduction in mortality.[135, 149-157] Additional studies also found continuity of care was associated with fewer hospital days, fewer intensive care days, and shorter length of hospital stay.[157, 158]

The effects of continuity of care also appear to go beyond that of improvements in morbidity and mortality considering it is also posited to have several disease-specific effects. In those with diabetes, continuity of care has been shown to improve health related quality of life[135] and body mass index as well as blood glucose, blood pressure, and cholesterol levels.[130, 159-161] It has also been suggested that continuity of care may increase antihypertensive drug utilization in those with hypertension,[162] as well as improve blood pressure control.[163] Last, in patients with severe mental illness, continuity of care is associated with improved health related quality of life as well as better community functioning, lower severity of symptoms and greater service satisfaction.[164]

The benefits of continuity of care are hypothesized to operate through several mechanisms. First, coordination of care activities (such as orchestrating referrals, managing prescriptions, or ensuring that patient information is transferred clearly between physicians) is more common in those with continuity of care.[165] Furthermore, continuity of care has been associated with more frequent cancer screening and receipt of preventative services,[155] as well as better treatment adherence.[166, 167]

Although it is well known that continuity of care represents an important aspect of medical care, and multimorbidity is common and associated with poor health outcomes, few studies have evaluated the interplay between the two. This represents a large gap in evidence for the effective care of this population, given previous research has shown that patients with multiple chronic conditions are more likely to experience fragmented care (i.e., care that is neither continuous or coordinated).[167] Although the exact reason for fragmented care in those with multimorbidity is unknown, one leading hypothesis is that the management of multimorbidity can often involve multiple clinicians.[168] Visiting multiple healthcare providers across a range of settings can lead to poor medical care through duplicative testing as well as conflicting medical advice, lack of communication, and treatment with multiple pharmacologic agents (increasing the risk for adverse drug events).[32, 36, 109] Thus, continuity of care has the potential to engender the suboptimal care a patient might receive as a result of their multimorbidity, however, there have been few attempts to investigate the potential relationship between continuity of care, multimorbidity and health outcomes.

1.2 Summary

In summary, chronic disease is the leading cause of death worldwide and its prevalence is expected to steadily increase. Because chronic conditions share interrelated risk factors, most patients with chronic disease tend to have many co-existing chronic conditions, also known as multimorbidity. Multimorbidity is not only associated with significant morbidity and mortality, it is also linked to decreased health related quality of life and impaired functional status, as well as an increased burden on the healthcare system.

Although multimorbidity is well known to be an important marker of poor outcomes in people with chronic disease, its impact in acute disease is relatively unknown. Moreover, there is little evidence for strategies which may improve care for patients at high risk of multimorbidity. Thus, this program of research aimed to evaluate the impact of multimorbidity on adverse outcomes in patients that survive an acute event, as well as to assess the interplay between continuity of care and multimorbidity to help inform approaches to management in this very high risk population.

1.3 Objectives

1) To determine the impact of multimorbidity on short term morbidity and mortality in patients managed for an acute hospital event;

2) To evaluate the impact of continuity of care and multimorbidity on short term morbidity and mortality in patients with chronic disease

1.4 Program of Research

Two manuscripts contributed to the overall study goals. The first study (Chapter 2) was a prospective cohort study that explored the relationship between multimorbidity and adverse health outcomes in a population-based cohort of adults who survived an episode of CAP. Admission for an acute condition, such as pneumonia, provides the ideal setting to study this research question given that several chronic conditions tend to cluster in this patient population and the risk of adverse events post- pneumonia discharge is very

high.[161] This study utilized data from a large, prospectively collected, well-validated population based cohort of patients with CAP.

The second study (Chapter 3) was a population based retrospective cohort study that evaluated the impact of continuity of care and multimorbidity on health outcomes in patients with diabetes. This study utilized data from the i3 inVision Drug Data Mart database from the United States, which provides longitudinal patient level data from a representative sample of patients insured by Medicare, Medicaid and commercial insurance plans. Data are collected directly from the clinical encounters, and include demographic information as well as laboratory test orders and results, physician and facility claims, as well as pharmacy claims data.

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CHAPTER 2: MULTIMORBIDITY IN ACUTE DISEASE

2.1 Introduction

Multimorbidity (i.e., an emerging concept most commonly defined as the coexistence of two or more chronic health conditions) is very common; and fully 25% of all adults seeking medical care, and about 3 in every 4 individuals aged 65 years or older, have multimorbidity.[1] This is a major concern for governments and healthcare systems, given that patients with multimorbidity represent an increasing burden on the healthcare system in terms of both cost and utilization.[2-4] Multimorbid patients are more likely to die prematurely, have poorer quality of life, and experience a greater loss of physical functioning than those without multimorbidity.[5-7]

Historically, researchers have tended to focus on the study and treatment of discrete disease states in those hospitalized for conditions such as heart failure, COPD and diabetes; this tendency is particularly pronounced in the study of acute conditions, like pneumonia. However, several chronic diseases cluster in patients with CAP,[8] and thus it provides an ideal condition to study the impact of multimorbidity on outcomes after hospital or ED discharge. CAP is one of the most common acute conditions in adults (particularly in the elderly) and is associated with high rates of hospitalization and mortality.[9,10] Furthermore, some studies suggest CAP may be associated with long-term sequelae such as ongoing respiratory problems,[11] cardiac complications, or other adverse effects,[12] and fully half of adults that survive a pneumonia hospitalization will be dead

within 5 years.[13] Although the Pneumonia Severity Index (PSI) includes some chronic conditions in its calculation, evaluating the independent effect of multimorbidity is important, given that age largely drives the PSI score and often many of the other criteria (e.g., laboratory data) are not immediately available to clinicians at the time of triage (site-of-care) decisions.[14-16] Therefore, our aim was to explore the relationship between multimorbidity and adverse health outcomes (death, hospitalization, ED visits) in a population-based cohort of adults who survived an episode of CAP.

2.2 Methods

Patients and Setting

Our prospective cohort has previously been described in detail.[13] In brief, data were collected prospectively for all patients 17 years or older with CAP who visited any of the 6 hospitals (inpatients) or were managed and discharged from the 7 ED's (outpatients) within Edmonton, Alberta, Canada from 2000 to 2002. All patients were treated according to a previously validated CAP critical pathway.[17, 18] CAP was defined as the presence of radiographic evidence of pneumonia determined by the treating physician and at least two of the following signs or symptoms: cough (productive or non-productive), pleurisy, shortness of breath, temperature>38°C, and crackles or bronchial breathing on auscultation. Patients with tuberculosis, cystic fibrosis, or who were immunocompromised, pregnant or nursing, or had been hospitalized in the previous 14 days were excluded from the cohort. In addition, we excluded all patients who died during the initial CAP episode and those with healthcare-associated pneumonia such as

nursing home residents. The study was approved by the Health Ethics Review Board of the University of Alberta (Edmonton, Alberta, Canada; approval #Pro00004999).

Measurements

Using standardized abstraction forms, trained research nurses collected all data including socio-demographic variables, comorbidities, and prescription medication use in the week prior to admission, as well as functional status, smoking status, and laboratory data. In addition, the well-validated PSI was calculated for each patient at the time of presentation. The PSI is a measure of pneumonia specific illness severity designed to predict 30-day all cause mortality and is based on demographics, co-morbidities, physical findings and laboratory tests.[14-16] While designed to predict 30-day mortality, we and others have demonstrated that the PSI can be used for risk-adjusted mortality for up to 5-years[13] and that the PSI is independently associated with both short and long term hospital readmissions.[13,19]

Multimorbidity

Patients were considered 'multimorbid' if they had at least two chronic conditions documented during their episode of CAP. Multimorbidity status was ascertained by determining the number (0, 1, 2, 3 or more) of existing physician-assigned diagnoses documented during the initial CAP presentation according to medical records and patient or proxy interviews. Chronic conditions included a history of any non-skin cancer,

chronic liver disease, heart failure (HF), stroke, ischemic heart disease, chronic kidney disease (CKD), end-stage renal disease requiring dialysis (ESRD), asthma, COPD, diabetes, seizures, and neuro-psychiatric disorders (see table 2-4 for distribution of chronic conditions). These conditions were included as they are required to calculate the PSI as well as commonly used comorbidity indices that predict 1-year mortality such as the Charlson Comorbidity Index, Elixhauser Index, and Mortality Risk Score.[20-23]

Outcomes

Our primary outcome of interest was all-cause death or hospital admission within 90-days of discharge from hospital or the ED. Our secondary outcomes included the components of the primary outcome (death or hospital admission separately) as well as ED visits. Ninety day outcomes were considered as this ensures that any adverse events observed might still be plausibly related to the original pneumonia episode and because this timeframe has been commonly used by others.[24, 25] All post-discharge data were ascertained using multiple linked and well-validated Alberta provincial administrative databases.[26] The quality and validity of these databases are routinely checked both provincially and federally with processes to resolve data issues where identified.

Analysis

Time-to-event data were plotted and calculated using Kaplan-Meier curves. Multivariable Cox proportional hazards models were used to estimate the independent association

between multimorbidity (defined as 2 or more chronic conditions) and our outcomes of interest adjusted for age, sex, site-of-care for the index CAP (inpatient or outpatient), premorbid functional status (defined as completely independent in ambulation and mobility vs not) and the PSI calculated at the time of presentation. Because the PSI score includes points for patients with the presence of certain chronic conditions (any non-skin cancer, any degree of CKD, heart failure, chronic liver disease, and stroke), we excluded these point values and recalculated an "acute" PSI (aPSI) score (based on physical examination, laboratory, and radiographic findings at presentation) as previously done by others.[19] Patients were followed for 90-days after their index CAP discharge from hospital or ED until death, first hospitalization, or emigration from the province. Proportional hazard assumptions were verified using Schoenfeld Residuals and no violations were observed. [27] No clinically or statistically important first order interaction terms were noted and none were included in final models.

Sensitivity Analyses

First, we evaluated the impact of the total number of comorbid conditions by further categorizing patients as having only 1 chronic condition, only 2 chronic conditions, or 3 or more chronic conditions compared to having no chronic conditions. Next, we repeated our analyses following patients from time of hospital admission to event of interest rather than from time of hospital discharge (as was done in the primary analysis) to allow for the inclusion of patients who died during the initial CAP encounter. Third, we evaluated whether or not the inclusion of the unmodified PSI (i.e., the conventional PSI which

includes comorbidity points for some conditions) would result in any changes to our main results. Last, given that our outcome was measured over a relatively short time period and censoring/loss to follow-up was minimal, we re-conducted our primary analysis using a logistic regression framework to determine the consistency of our results. All analyses were conducted using STATA/SE version 12.0 (Stata Corp College Station,TX, USA).

2.3 Results

Patient Characteristics

Of the 6,874 patients with CAP, 321 (5%) patients died in hospital and were excluded from primary analyses, as were 367 (6%) patients who could not be linked to administrative databases and 621 (10%) nursing home residents, resulting in a final cohort of 5,565 patients. Mean age was 57 (SD 20) years, 2,240 (40%) were 65 years of age or older, 2,977 (54%) were male, 3,283 (59%) were treated as outpatients (i.e., treated for CAP and discharged to the community from the ED), 5,054 (91%) were functionally independent prior to their CAP, mean PSI was 75 (SD 39), and 1,649 (30%) had severe (PSI Class IV or V) pneumonia. The mean aPSI was 15 (SD 21) after the subtraction of points for age and comorbidities.

Prevalence and Correlates of Multimorbidity

Overall, 1,602 (29%) patients had multimorbidity as we defined it. Specifically, 2,378 (43%) patients had no chronic conditions, 1,585 (29%) had one chronic condition, 831 (15%) had two chronic conditions, and 771 (14%) had three or more chronic conditions.

Compared to those without morbidity, patients with multimorbidity were significantly older, more likely to be treated as inpatients, less likely to be functionally independent and tended to have more severe pneumonia (Table 2-1).

All-Cause Death or All-Cause Hospital Admission after index CAP event

Overall, of the 5,565 patients who survived their initial hospitalization or ED assessment, 255 (5%) subsequently died and 1,101 (22%) were (re)admitted to hospital within 90 days. Multimorbidity was associated with significant increases in the risk of death or hospitalization within 90 days (37% vs 17%, adjusted hazards ratio [aHR]: 1.43, 95% CI: 1.26-1.62) as well as for each endpoint separately (7% vs 1%, aHR: 3.02, 95% CI: 1.98-4.62 for death within 90-days of CAP discharge; 35% vs 16%, aHR: 1.43, 95% CI: 1.26-1.63 for hospital admission within 90-days of CAP discharge). (Table 2-2)

Emergency Department Visit after index CAP event

Overall, 2,049 (37%) of those with pneumonia who were discharged from hospital or ED presented back to an ED within 90-days. Compared to those who did not have multimorbidity, those with multimorbidity were 40% more likely to visit the ED within 90-days of discharge (45% vs 34%, aHR: 1.40, 95% CI: 1.26-1.56).

Sensitivity Analyses

First, in terms of dose-response, the existence of each chronic condition was associated with a graded and increased risk of death or hospital admission, death alone, hospital admission alone, and ED visits (adjusted p-value for trends all <0.001, Table 2-3, Figure 2-1). Indeed, the existence of three or more chronic conditions in patients with CAP was associated with a 2-fold increased risk in 90-day death or all-cause hospitalization when compared to those without any chronic conditions (42% vs 12%, aHR: 2.13, 95% CI: 1.76-2.58). Second, our results were nearly identical to our main study findings after including patients who died during the initial CAP event, in that multimorbidity was still associated with a 38% increased risk of death or hospital admission (aHR: 1.38, 95% CI: 1.22- 1.55). Additionally, inclusion of the unmodified PSI (which contained points for several chronic conditions) attenuated the relationships observed, although multimorbidity was still independently associated with a 14% relative increase in the risk of death or hospital admission (aHR: 1.14, 95% CI: 1.00-1.30, p=0.045). Last, we found similar results to that of our main analysis using a logistic regression framework (adjusted odds ratio for multimorbidity present vs absent: 1.60, 95% CI: 1.34-1.82).

2.4 Discussion

In our large population-based cohort of CAP patients, 29% of patients had multimorbidity as currently defined. We found that multimorbidity was associated with approximately a 40% increased risk of death or hospital admission 90-days following discharge from the CAP index event. Furthermore, a strong graded relationship existed between the number of comorbidities and adverse outcomes. Although multimorbidity is

often classified as 2 or more chronic conditions, we observed that in the case of pneumonia, even the presence of one chronic condition was associated with significantly increased rates of adverse events. To our knowledge, our study is one of the first to explore multimorbidity in the setting of pneumonia; but whether or not our findings can be generalized to other acute illness episodes is not yet known.

It is important to point out that although the PSI includes a weighted score for some chronic conditions,[13] we found that the number of chronic conditions patients had independently predicted short-term adverse outcomes even after adjustment for PSI scores. This may be especially important to consider in settings such as the ED, where site-of-care and other triage decisions must be made quickly and often without the availability of a complete medical history and all requisite laboratory data. In addition, the PSI requires "weighting" the scores of specific comorbidities while other triage risk scores such as the CURB-65 (based on confusion, urea levels, respiratory rate, blood pressure and age), CTAS (Canadian Triage and Acuity Scale), SOAR (based on systolic blood pressures, oxygenation, age and respiratory rate), and SMART-COP (based on blood pressure, multilobar involvement, albumin levels, respiratory rate, tachycardia, confusion, oxygenation and PH) do not account for chronic conditions. Indeed, even after adjustment for the regular PSI, multimorbidity was still associated with an approximately 14% increased risk of death or hospital admission, which suggests that a simple count of chronic conditions is prognostically relevant.

Although our study has several strengths, including the evaluation of both inpatient and outpatients, a large population-based sample, and detailed clinical data collected by chart review rather than just administrative records, there are a few limitations. First, this was an observational study and residual confounding is always a potential issue with observational studies. Considering the richness of our data source, however, we were able to adjust for a number of important patient-level confounders including the well-validated PSI risk score. Second, we were unable to identify changes in clinical parameters over time; however our follow-up time was relatively short so this should not be important. Lastly, standard definitions of multimorbidity, which we used, do not permit any relative weighting of the importance of particular conditions (e.g., current heart failure vs remotely treated colorectal cancer) or the severity of any specific condition (e.g., well controlled diet treated diabetes vs brittle diabetes requiring an insulin pump).

In summary, in our study of patients with pneumonia, multimorbidity was very common and provided important prognostic information for the post-discharge period. While the management of a life-threatening acute illness always take clinical priority, our findings suggest that when managing or making site-of-care decisions for patients with pneumonia, more attention should be paid to apparently "unrelated" comorbidities and multimorbidity. Given the strong association with short-term adverse events, perhaps these chronic diseases are more "related" than previously appreciated and need to be considered when deciding on readiness for discharge to the community.

Table 2-1: Characteristics of 5,565 patients after an episode of community acquired pneumonia stratified by multimorbidity status

Characteristic	Full Cohort (n=5,565)	Less than two chronic conditions (n=3,963)	Multimorbidity (Two or more chronic conditions) (n=1,602)	P-value*
Age (Mean ± SD)	56.8 (20.3)	52.2 (19.6)	70.8 (14.2)	<0.001
≥ 65 years n (%)	2,240 (40.3)	1,101 (27.8)	1,139 (71.1)	<0.001
Male n (%)	2,977 (53.5)	2,088 (52.7)	889 (55.5)	0.057
Outpatient n (%)	3,283 (59.0)	2,824 (71.3)	459 (28.7)	<0.001
Functional Independence n (%)	5,054 (90.8)	3,624 (91.5)	1,430 (89.3)	0.01
Acute Pneumonia Severity Index (Mean ± SD)	14.7 (21.0)	10.3 (17.1)	25.5 (25.4)	<0.001
Pneumonia Severity Index (Mean ± SD)	71.7 (37.5)	58.6 (31.0)	103.9 (32.2)	<0.001

*P-value is for difference between less than two chronic conditions and two or more chronic conditions

Table 2-2 : Unadjusted and adjusted hazard ratios for primary and secondary outcomes within 90-days according to multimorbidity status

90-day Outcomes	Multimorbidity (Two or more chronic conditions)	Crude event rate n (%)	Unadjusted HR (95% CI)	Adjusted HR* (95% CI)	P-value for Adjusted HR
All Cause Death or Hospital Admission					
	Absent	685 (17.3)	Reference	Reference	
	Present	595 (37.1)	2.41 (2.16-2.69)	1.43 (1.26-1.62)	<0.001
All Cause Death					
	Absent	28 (1.2)	Reference	Reference	
	Present	227 (7.1)	6.25 (4.22-9.30)	3.02 (1.98-4.62)	<0.001
All Cause Hospital Admission					
	Absent	649 (16.4)	Reference	Reference	
	Present	556 (34.7)	2.38 (2.12-2.66)	1.43 (1.26-1.63)	<0.001
Emergency Department Visit					
	Absent	1,336 (33.7)	Reference	Reference	<0.001
	Present	713 (44.5)	1.39 (1.27-1.52)	1.40 (1.26-1.56)	

*HR is adjusted for age, sex, aPSI, setting, functional status

Table 2-3: Unadjusted and adjusted hazard ratios for all cause death or hospital admission within 90-days according to multimorbidity count

90-day Outcomes	Number of Chronic Conditions	Unadjusted HR (95% CI)	Adjusted HR* (95% CI)	P-value for trend†
All Cause Death or Hospital Admission				
	0	Reference	Reference	<0.001
	1	2.23 (1.91-2.59)	1.68 (1.43-1.97)	
	2	3.09 (2.62-3.65)	1.90 (1.58-2.28)	
	3+	4.08 (3.48-4.79)	2.13 (1.76-2.58)	
All Cause Death				
	0	Reference	Reference	<0.001
	1	4.39 (2.86-6.76)	2.76 (1.77-4.33)	
	2	7.31 (4.71-11.33)	3.36 (2.09-5.39)	
	3+	9.00 (5.85-13.86)	3.34 (1.88-5.43)	
All Cause Hospital Admission				
	0	Reference	Reference	<0.001
	1	2.18 (1.87-2.55)	1.66 (1.41-1.96)	
	2	3.01 (2.54-3.58)	1.88 (1.56-2.27)	
	3+	3.97 (3.37-4.67)	2.13 (1.75-2.58)	
Emergency Department Visit				
	0	Reference	Reference	<0.001
	1	1.23 (1.10-1.37)	1.28 (1.14-1.43)	
	2	1.44 (1.27-1.63)	1.52 (1.32-1.75)	
	3+	1.60 (1.41-1.82)	1.75 (1.51-2.05)	

*****HR is adjusted for age, sex, aPSI, setting, functional status

†For trend across increasing number of chronic conditions

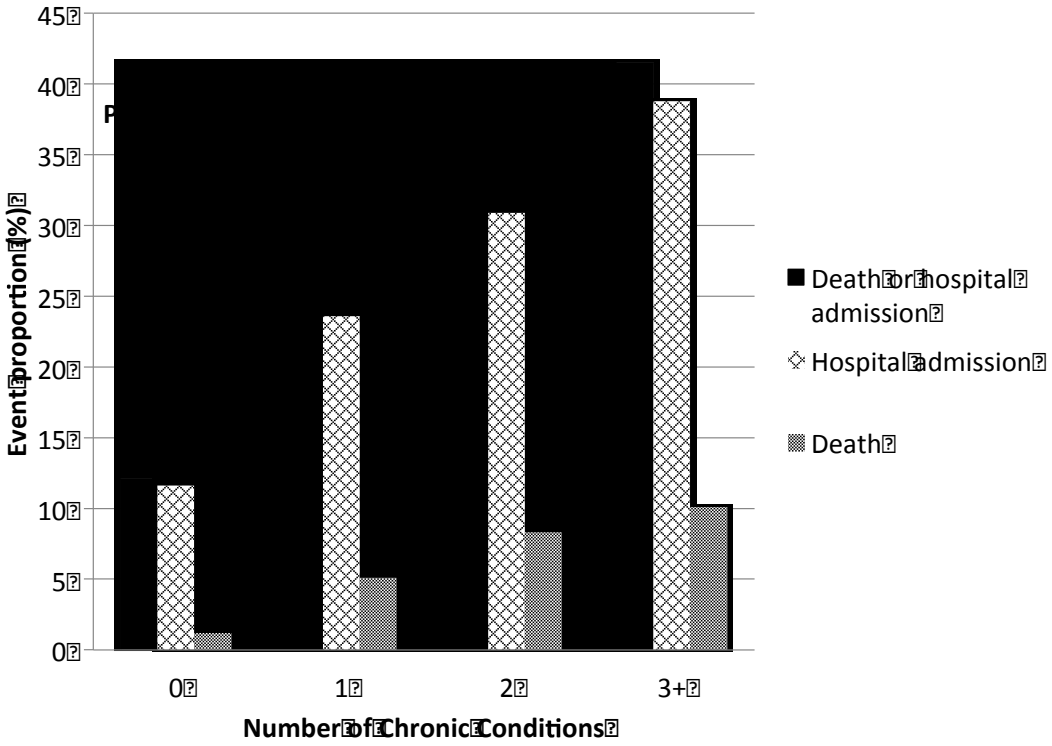
Table 2-4: Distribution and prevalence of chronic conditions at time of community acquired pneumonia episode

Chronic Condition*	Crude number	% of all patients with CAP (n=5,565)	% of patients with multimorbidity (n=1,602)
Non-skin cancer	487	8.8	30.4
Chronic liver disease	125	2.3	7.8
Heart failure	432	7.8	27.0
Stroke	290	5.2	18.1
Ischemic Heart Disease	1,071	19.2	66.9
Kidney Disease†	352	6.3	21.9
Asthma	732	13.2	45.7
Chronic obstructive pulmonary disease	921	16.7	57.5
Diabetes	569	10.2	35.5
Seizure	124	2.2	7.7
Neuro-psychiatric disorder	428	7.7	26.7

*** Chronic condition categories are not mutually exclusive; individuals can have more than one chronic condition**

†Includes both chronic kidney disease and end-stage renal disease requiring dialysis

Figure 2-1: Risk of death or hospital admission for 5,565 patients 90-days after discharge for an episode of community acquired pneumonia by multimorbidity status



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CHAPTER 3: MULTIMORBIDITY IN CHRONIC DISEASE

3.1 Introduction

Globally, diabetes is one of the most common chronic non-communicable diseases, and in North America it affects 7% of individuals and it is a leading cause of death.[1] The complexity of care for patients with diabetes is increasing in part due to the growing prevalence of co-existing chronic conditions.[2] Most patients with diabetes have multimorbidity (i.e., at least one other chronic condition),[3] and as many as 25% have four or more concurrent chronic conditions.[4, 5]

Previous studies suggest that patients with diabetes and multimorbidity experience poorer health outcomes compared to those with diabetes alone.[6, 7] For instance, in heart failure, patients with diabetes had a 29% increased risk of death compared to patients without diabetes[8] and those with both diabetes and chronic kidney disease had a 34% increased risk of death compared to those with diabetes alone.[9] It has been hypothesized that one of the factors contributing to worse outcomes for patients with multimorbidity is fragmentation of care.[10] At least for heart failure, continuity of care (the ongoing or consistent relationship between a patient and physician) has been shown to be associated with reduced risk of death and hospital admission.[11] This phenomenon has been documented in multiple conditions although the mechanisms remain poorly understood as does the impact of multimorbidity.[10, 12]

As the majority of patients with diabetes have multimorbidity, these patients tend to receive care from multiple providers (e.g., general practitioners, endocrinologists, cardiologists, nephrologists, other internal medicine specialists, etc.).[13] While studies have demonstrated that continuity of care may improve certain components of diabetes care such as control of glucose, blood pressure, cholesterol, and perhaps be associated with improvements in health related quality of life, the impact of continuity on broader clinical events such as death or all-cause hospitalizations is uncertain.[14-22] Further, it is unknown what role continuity of care plays in the context of multimorbidity in patients with diabetes and therefore we undertook the present investigation in a large cohort of insured patients with incident diabetes and examined 1-year outcomes.

3.2 Methods

We conducted a population-based, cohort study using a large US claims database that includes employed, commercially-insured individuals as well as those insured through Medicare and Medicaid from all 50 states (Clinformatics Data Mart, OptumInsight Life Sciences Inc). [23] Patient data is updated every 90-days and was de-identified and accessed using protocols compliant with the Health Insurance Portability and Accountability Act. Patient level data included administrative and demographic information (type of insurance plan, income, sex, age, dates of eligibility), billable medical services claims including inpatient and outpatient visits and medical procedures (physician and facility identifier, date and place of service, cost of service, admission, and discharge dates, procedures and diagnostic codes), all laboratory tests and results (including fasting lipids, renal function, liver function, glycosylated hemoglobin, and complete blood count) and

pharmacy claims data (prescribing physician, drug dispensed based on national drug codes, quantity and date dispensed, drug strength, days supply, cost of service). All clinical diagnoses were recorded according to ICD-9-CM (international classification of diseases, 9th revision, clinical modification) codes and procedure codes (according to ICD-9 and current procedural terminology 4 codes). [24-27]

Cohort selection

Overall, 429,512 patients with incident diabetes were identified based on physician claims, hospital discharge abstracts, and/or ambulatory care visits based on ICD-9 CM codes between January 1, 2004 and December 31, 2009. Specifically, incident diabetes was defined as at least 1 hospitalization or 2 physician claims with a diabetes specific ICD-9 code (250.XX), over a 2-year period or a first claim for an oral antihyperglycemic drug or insulin, and no history of diabetes codes or diabetes drug therapy in the previous 2 years.[28] Patients had to be at least 20 years of age and have at least two years of continuous medical insurance to be eligible for the study. Those who had less than two years of follow-up following incident diabetes were excluded.

Continuity of Care – defined within first two years following incident diabetes

Continuity of care was defined using Breslau's Usual Provider of Continuity (UPC). The UPC measure was chosen as it is well validated, easily understood, and most commonly found in the literature.[29] UPC was calculated as n/N in the 2-years following the

diagnosis of incident diabetes; where n was the number of primary or specialist care visits (excluding pregnancy related visits) from an individual's most responsible health care provider and N was the total number of primary and specialist health care visit.[17] The most responsible health care provider was defined as the physician that a patient visited the greatest number of times in the two years after the incident date for diabetes diagnosis.[29-31] Both primary care (family practitioners, general practitioners, and general internists) and specialists (endocrinology, non-endocrinology internal medicine subspecialties, surgery, and surgical subspecialties - see table 3-4) were eligible to be considered as an individual's most responsible care provider given that patients with diabetes often see specialists regularly and may even consider them as their primary care physician.[32, 33] Since the UPC estimate is unstable in those with limited physician encounters, we excluded all patients who did not have at least four physician visits during the two years following incident diabetes diagnosis (Figure 3-1).[34-36] As per convention in this literature, patients were defined as having good provider continuity if their UPC measure was ≥75% (i.e., the same specialist or primary care provider was responsible for three quarters of all visits)[17, 35]

Multimorbidity

Multimorbidity was ascertained by determining the number of comorbid conditions patients were diagnosed with (ICD-9 codes for physician claims, hospital admission and emergency department visits), in the 2-years after their new diabetes diagnosis. The 17 conditions included were those found in the Charlson Comorbidity Index, Elixhauser

Comorbidity Index, and Mortality Risk Score (see table 3-5).[37-40] Patients had multimorbidity if they had at least one other chronic condition in addition to diabetes.[41]

Outcomes – based on events between years 2 and 3 following incident diabetes diagnosis

We began 1-year follow-up for outcomes 2-years after the first diabetes diagnosis (Figure 3-2). Our primary outcome of interest was the composite endpoint of all-cause death or hospital admission during that year. In essence, we determined if continuity of care over a 2-year period following new diabetes predicted outcomes during year 3; by design, every patient thus had 3-years of observation, 2-years to define UPC, and 1-year of follow-up for outcomes thereafter. Our secondary endpoints included the components of our composite (all-cause death and hospital admission individually). Vital status was determined through linkage to the US national death index files (although cause of death was not ascertained).[19, 42] Linkage to this index is highly reliable and valid when social security numbers are available, as in our case (greater than 98% specificity).[19,43]

Statistical Analysis

Patient characteristics were reported as means and standard deviations for continuous variables and proportions for categorical variables. Student t-tests and chi^2 tests were used to compare characteristics between those with good provider continuity (UPC ≥75%) and those without (UPC <75%). We evaluated the independent effects of continuity of care and multimorbidity on our outcomes of interest using multivariable logistic regression analysis. Covariates in our models included sociodemographic characteristics (age, sex, income) and adjusted clinical groups derived from the John

Hopkins ACG system.[44] These included the number of inpatient hospitalizations patients had in the two years following diabetes diagnosis, as well as a frailty flag. This flag is assigned (using the ACG methodology) to individuals who had at least one of the following diagnoses in the two years following incident diabetes: malnutrition, dementia, impaired vision, decubitus ulcer, incontinence, loss of weight, obesity, poverty, barriers to access of care and difficulty walking.[44] Additional covariates included laboratory data (A1c, cholesterol levels, estimated glomerular filtration rate [stratified into ≥60, 59.9-30, <30ml/min], albuminuria, hemoglobin), and prescription drugs (antiplatelet drugs, anticoagulants, statins, calcium channel blockers, β-blockers, angiotensin converting enzyme inhibitors, diuretics, nitrates, antidiabetic agents [metformin, sitagliptin, sulfonylureas, thiazolidinediones, insulin]). All covariates were defined based on the most recent value available before follow-up for 1-year outcomes began. For patients who were missing clinical laboratory information, we used the missing indicator approach. [45]

Sensitivity Analyses

First, we determined the impact of continuity of care in those with and without multimorbidity. Next, we examined different UPC cut-offs, specifically the impact of UPC between ≥30-<60% and UPC≥60% compared to UPC<30% on our primary outcome. Third, we determined whether our results were robust across different definitions of most responsible provider (i.e., specialist care or primary care physician). Fourth, in order to try and address the issue of confounding by diabetes severity ("by

indication"), we conducted a separate analysis in those with poor glycemic control (A1c values above 7.5%). Next, again to try and address confounding by severity, we directly adjusted for the number of healthcare visits during the 2-years which the UPC was defined.[10] Last, given that our outcome was measured over a one-year period and some patients were censored prior to study end, we re-conducted our primary analysis using Cox proportional hazards modelling to account for censoring/loss to follow up.

3.3 Results

We identified 285,231 patients with incident diagnosis of diabetes who met our inclusion criteria. Mean age was 53 (SD 11), 140,032 (49%) were female, and 212,185 (74.4%) had multimorbidity (Table 3-1): 44.1% had one comorbid condition in addition to diabetes, 18.4% had two additional conditions, and 11.9% had three or more additional chronic conditions. The three most common comorbid conditions were hypertension, angina and stroke. In the 2-years following new diabetes diagnosis, mean UPC was 0.59 (SD 0.21) and 77,270 (27.1%) of patients were defined as having good provider continuity (UPC≥75%). Overall, the average number of physician visits during the 2-years when the UPC was calculated was 21 (SD 21) with a mean of 9 (SD 6) different physicians. During the 1-year follow-up period in which outcomes were ascertained (i.e., within year 3 after incident diabetes), 33,632 (11.8%) patients died or were hospitalized for any cause; 850 (0.3%) died, and 30,495 (10.7%) were hospitalized.

Overall, we found that in the 2 years after diabetes diagnosis, those with good provider continuity (n=77,270, 27%) had far fewer physician visits, were younger, were less likely to be female, were less likely to be frail, were less likely to be treated with diabetes and cardiovascular medications, and were less likely to be hospitalized (2.5% vs. 18.1%) compared to those with less provider continuity (n=207,961, 73%) (Table 3-1). Good provider continuity in years 1 and 2 was independently associated with a reduced risk of all cause death or hospitalization in year 3 compared to those without good provider continuity (7.2% vs 13.5%, adjusted odds ratio [aOR]: 0.72, 95% CI: 0.70-0.75), and findings were consistent for each component of our primary endpoint (Table 3-2). In the same model, the presence of multimorbidity was also independently associated with an increased risk of 1-year composite outcomes (13.4% vs 7.2% for those without multimorbidity, aOR: 1.26, 95% CI: 1.21-1.30) as well as for death and hospital admission separately (Table 3-3).

Sensitivity Analyses

First, stratified analyses according to multimorbidity status showed results similar to the overall model (Figure 3-3). In those without multimorbidity, good continuity of care was associated with a 25% lower risk of death or hospital admission (5.7% vs 8.0%, aOR:0.75, 95% CI:0.71-0.80). In those with multimorbidity, continuity of care was associated with a 29% lower risk of death or hospitalization (7.9% vs 15.2%, aOR: 0.71, 95% CI: 0.69-0.74) (p=0.18 for interaction). Next, our results were stable to altering of our UPC cut-offs. Using those with UPC<30% as the referent group, UPC≥60% (aOR: 0.59, 95% CI:

0.57-0.62) and 30%≤UPC<60% (aOR: 0.77, 95% CI: 0.74-0.80) were associated with decreased risk of subsequent death or hospital admission. Next, we found that our results were similar to that of our main analysis after stratification by most responsible provider. For those with specialists as their most responsible provider (n=39,885, 14%), better continuity of care (UPC≥75%) was associated with a decreased risk of death or hospital admission (aOR:0.70, 95% CI: 0.63-0.77) – similar to the results for those with a primary care physician as their most responsible healthcare provider (n=173, 651, 61%): aOR 0.76 (95% CI: 0.74-0.79). Additionally, we found that continuity of care was still associated with improved health outcomes even in those with more severe disease. For example, continuity of care was associated with a 26% decreased risk of death or hospital admission in those with A1c levels greater than 7.5 (aOR: 0.74, 95% CI: 0.68-0.80) and a 20% decreased risk of our primary outcome after adjustment for the number of physician visits in the two years in which UPC was defined (aOR: 0.80, 95% CI: 0.77-0.83). Last, we found similar results for the effect of continuity of care on our primary outcome utilizing a survival analysis framework (aHR: 0.80, 95% CI: 0.78-0.83).

3.4 Discussion

Our study found that better continuity of care was associated with lower rates of subsequent death or all-cause hospitalization in patients with diabetes, and that although multimorbidity was independently associated with an increased risk of the primary composite endpoint, the benefits of continuity were similar in those with and without multimorbidity. As multimorbidity is common in patients with diabetes (three-quarters

of all patients in our cohort had multimorbidity), our results suggest that all patients with diabetes may benefit from better continuity of care.

Our results are consistent with other studies evaluating the impact of continuity of care on health outcomes in the diabetes population. In two retrospective cohort studies of elderly people with diabetes, those with higher physician continuity had lower risk of hospitalization (53.5% vs 68.2%) and death (8.6% vs 18.5%) [17] as well as decreased rates of hospital admission (rate ratio: 0.82).[16] We have extended this literature to show that continuity of care is beneficial whether diabetes patients do or do not have other chronic conditions.

Although our study has many strengths such as the inclusion of specialist care visits, a large population based sample of patients from both commercial and Federal insurance plans and adjustment for detailed clinical, lab and drug information not available to most studies on continuity of care, there were limitations. First, patients who are 'sicker' are more likely to see a greater number of physicians, resulting in lower continuity scores for these patients, thus potentially explaining the association between low provider continuity and poor health outcomes. However, this hypothesis has proved difficult to examine using randomized clinical trials and thus observational data is likely to produce the majority of the evidence that can be brought to bear to answer this question. Second, as administrative data was utilized, we do not know why patients went to visit a physician, whether visits were initiated by patients or physicians, or whether there were any co-pays

or penalties associated with these visits, all of which could influence health care utilization and physician continuity. Third, we only looked at average continuity over a two year period following a new diabetes diagnosis and excluded those who died during this period; therefore, we were not able to evaluate the potential effect of continuity on early health outcomes. We did, however, assume that patients' continuity of care would remain relatively stable over this two year period. Last, missing data was a limiting factor that may have impacted the validity of our results. Although we utilized the missing indicator approach in order to account for this limitation, it may not have been adequate[46] and other methods, such as simple imputation [47] or multiple imputation [48] were not completed. There is, however, no universally accepted method for handling missing data that has unequivocally been shown to produce unbiased results. Furthermore, as we only included those individuals with complete information on HbA1c in our sensitivity analyses, missing data may have affected these estimates.

In summary, we found an independent association between better continuity of care and a lower risk of subsequent death or all-cause hospitalizations, an increased risk of our primary endpoint (state what the primary endpoint was) in those with multimorbidity, and that continuity is beneficial in those with diabetes whether or not they have multimorbidity. Our study supports the role for continuity of care as one of the fundamental building blocks for any high-performing healthcare system and suggests that clinicians and health care systems should continue to develop mechanisms to optimize continuity of care for all patients with diabetes.

Table 3-1: Characteristics in the two years following incident diabetes according to provider continuity status

Characteristics	Overall (n=285,231)	UPC<75% (n=207,961)	UPC≥75% (n=77, 270)	P-value*
Age, mean (SD)	53.0 (10.5)	53.8 (10.4)	51.0 (10.4)	<0.001
Over the age of 65yrs, n (%)	29, 640 (10.4)	24,093 (11.6)	5,547 (7.2)	<0.001
Female, n (%)	140,032 (49.1)	109,033 (52.4)	30,999 (40.1)	<0.001
Income, mean (SD)	48,842 (6,567)	48,880 (6,626)	48,738 (6,402)	
Number of chronic conditions in addition to diabetes, n (%)				<0.001
0	73,046 (25.6)	48,429 (23.3)	24, 617 (31.9)	
1	125, 805 (44.1)	84,736 (40.8)	41, 069 (53.2)	
2	52,433 (18.4)	43,405 (20.9)	9,028 (11.7)	
3+	33,947 (11.9)	31,391 (15.1)	2,556 (3.3)	
Frailty	15,884 (5.6)	13, 403 (6.4)	2, 481 (3.2)	<0.001
Number of inpatient hospitalizations, mean (SD)	0.2 (0.62)	0.3 (0.70)	0.03 (1.9)	<0.001
Number of inpatient hospitalizations, n (%)				<0.001
0	245,440 (86.1)	170,134 (81.2)	75,306 (97.5)	
1	29,117 (10.2)	27,336 (13.1)	1,781(2.3)	
2+	10,674 (3.7)	10,491 (5.0)	183 (0.2)	
Estimated glomerular filtration rate category (mL/min):				<0.001
<30	2073 (0.9)	1,895 (0.9)	178 (0.2)	
30 to <60	28230 (12.1)	23,042 (11.1)	5,188 (6.7)	
≥60	202112 (87.0)	147,000 (70.7)	55,112 (71.3)	
Lab Values				
Mean (SD) total cholesterol (mg/dl)	187.3 (42.3)	187.0 (42.6)	187.9 (41.6)	<0.001
Mean (SD) triglycerides (mg/dl)	168.5 (156.5)	167.1 (153.8)	172.3 (163.9)	<0.001
Mean (SD) HDL cholesterol (mg/dl)	48.5 (14.0)	49.1 (14.0)	47.1 (13.0)	<0.001
Mean (SD) LDL cholesterol (mg/dl)	107.7 (34.6)	107.1 (34.7)	109.6 (34.2)	<0.001
Mean (SD) HbA1c (%)	7.0 (1.6)	6.9 (1.6)	7.1 (1.6)	<0.001
Mean (SD) hemoglobin (mg/dl)	14.0 (1.5)	13.9 (1.5)	14.3 (1.5)	<0.001
Drug Use				
Sitagliptin	6,432 (2.3)	4,626 (2.2)	1,806 (2.3)	0.071
Metformin	102,233 (35.8)	72,973 (35.1)	29,260 (37.9)	<0.001
Insulin	34,458 (12.1)	27,915 (13.4)	6,543 (8.5)	<0.001

Sulfonylurea	65,754 (23.1)	47,393 (22.8)	18,361 (23.8)	<0.001
Thiazolidinedione	55,740 (19.5)	39,839 (19.2)	15,901 (20.6)	<0.001
Other antidiabetic agent	11,529 (4.0)	8.921 (4.3)	2,608 (3.4)	<0.001
ACE inhibitor/ ARB	142,983 (50.1)	106,413 (51.2)	36,570 (47.3)	<0.001
Statin	135,936 (47.7)	101,667 (48.9)	34,269 (44.4)	<0.001
Beta blocker	71,500 (25.1)	57,611 (27.7)	13,889 (18.0)	<0.001
Dihydro calcium channel blocker	40,981 (14.4)	31,010 (14.9)	9,971 (12.9)	<0.001
Non-dihydro calcium channel blocker	17,177 (6.0)	13,635 (6.6)	3,509 (4.5)	<0.001
Nitrates	15,875 (5.6)	14,477 (7.0)	1,398 (1.8)	<0.001
Loop diuretic	24,496 (8.6)	21,322 (10.3)	3,174 (4.1)	<0.001
Anticoagulants	10,214 (3.6)	9,206 (4.4)	1,008 (1.3)	<0.001
Antiplatelet agents	16,505 (5.8)	15,151 (7.3)	1,354 (1.8)	<0.001
Phosphate inhibitors	22,419 (7.9)	16,314 (7.8)	6,105 (7.9)	0.62
Healthcare utilization two years following incident diabetes				
Number of unique physicians, mean (SD)	8.5 (6.4)	10.3 (6.5)	3.4 (1.4)	<0.001
Number of physician visits, mean (SD)	20.7 (21.0)	24.6 (22.6)	10.1 (9.9)	<0.001
Number of primary care visits, mean (SD)	9.0 (7.9)	9.7 (8.5)	7.2 (5.9)	<0.001
Number of specialist care visits, mean (SD)	11.7 (16.4)	14.9 (17.5)	3.0 (7.9)	<0.001
Number of internal med visits	4.9 (10.4)	6.3 (11.3)	1.3 (6.0)	<0.001
Number of endocrinologist visits	0.6 (2.1)	0.7 (2.3)	0.2 (1.1)	<0.001
Number of surgery and anesthesiology visits	5.7 (8.1)	7.3 (8.6)	1.4 (4.5)	<0.001
Number of other specialist visits	0.5 (1.4)	0.6 (1.6)	0.1 (0.7)	<0.001
Ratio primary care to specialist care visits, mean (SD)	2.2 (3.0)	1.3 (1.8)	4.8 (4.0)	<0.001

*** P-value is for difference between UPC< 75% and UPC≥75%**

Table 3-2: Outcomes according to provider continuity status

Outcome	Events-n(%)	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)	P-value Adjusted OR
All cause hospital admission or all cause mortality				
UPC < 75%	28,085 (13.5)	Reference	Reference	-
UPC ≥ 75%	5,547 (7.2)	0.50 (0.48-0.51)	0.72 (0.70-0.75)	<0.001
All cause death				
UPC < 75%	741 (0.4)	Reference	Reference	-
UPC ≥ 75%	109 (0.1)	0.40 (0.32-0.49)	0.75 (0.61-0.94)	0.01
All cause hospital admission				
UPC < 75%	25,575 (12.3)	Reference	Reference	-
UPC ≥ 75%	4,920 (6.4)	0.49 (0.47-0.50)	0.68 (0.66-0.70)	<0.001

*** Adjusted for demographics, clinical parameters, lab values and drug use**

Table 3-3 Outcomes according to multimorbidity status

Outcome	Events-n(%)	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)	P-value Adjusted OR
All cause hospital admission or all cause mortality				
Multimorbidity absent	5,286 (7.2)	Reference	Reference	-
Multimorbidity present	28,346 (13.4)	1.98 (1.92-2.04)	1.26 (1.21-1.30)	<0.001
All cause death				
Multimorbidity absent	42 (0.06)	Reference	Reference	-
Multimorbidity present	808 (0.4)	6.64 (4.87-9.07)	2.36 (1.70-3.29)	<0.001
All cause hospital admission				
Multimorbidity absent	5,093 (7.0)	Reference	Reference	-
Multimorbidity present	25,402 (12.0)	1.81 (1.76-1.87)	1.26 (1.21-1.31)	<0.001

*** Adjusted for demographics, clinical parameters, lab values and drug use**

Table 3-4 Subspecialties included within categories of specialties

Internal medicine and subspecialties, non-endocrinology

ALLERGY & IMMUNOLOGY
CARDIOLOGY
CRITICAL CARE MEDICINE
DERMATOLOGY
GASTROENTEROLOGY
GERIATRIC MEDICINE
HEMATOLOGY & ONCOLOGY
INFECTIOUS DISEASES
NEPHROLOGY
NEUROLOGY
PULMONARY MEDICINE
RHEUMATOLOGY
PHYSICAL MEDICINE & REHABILITATION

Endocrinology

ENDOCRINOLOGY

Surgery, anesthesia, and surgical subspecialties

ANESTHESIOLOGY
COLON & RECTAL SURGERY
GENERAL SURGERY
NEUROLOGICAL SURGERY
THERAPEUTIC RADIOLOGY
THORACIC SURGERY
UROLOGY
OPHTHALMOLOGY
ORTHOPEDICS
OTOLARYNGOLOGY
PODIATRY MD
VASCULAR SURGERY

Other (psychiatry, emerg, etc)

EMERGENCY MEDICINE
PSYCHIATRY
OSTEOPATHY

Table 3-5: Distribution and prevalence of chronic conditions within two year period following incident diabetes

Chronic Condition	Crude number	% of all patients with Diabetes (n=285,231)	% of patients w multimorbidit (n=212,231)
Hypertension	198,197	69.5	93.4
Myocardial infarction	4,555	1.6	2.1
Angina	51,415	18.0	24.2
Peripheral vascular disease	6,596	2.3	3.1
Cerebrovascular disease	18,991	6.7	8.9
Heart Failure	11,729	4.1	5.5
Chronic obstructive pulmonary disease	12,342	4.3	5.8
Asthma	14,759	5.2	7.0
Connective tissue disorder	2,663	0.9	1.3
Peptic ulcer disease	10,086	3.5	4.8
Chronic liver disease	3,932	1.4	1.9
Hemiplegia	1,082	0.4	0.5
Chronic renal failure	6,689	2.4	3.2
Any neoplasm	5,782	2.0	2.7
HIV/AIDS	792	0.3	0.4
Seizure	2,137	0.8	1.0
Dementia	856	0.3	0.4

Figure 3-1: Major exclusions from study

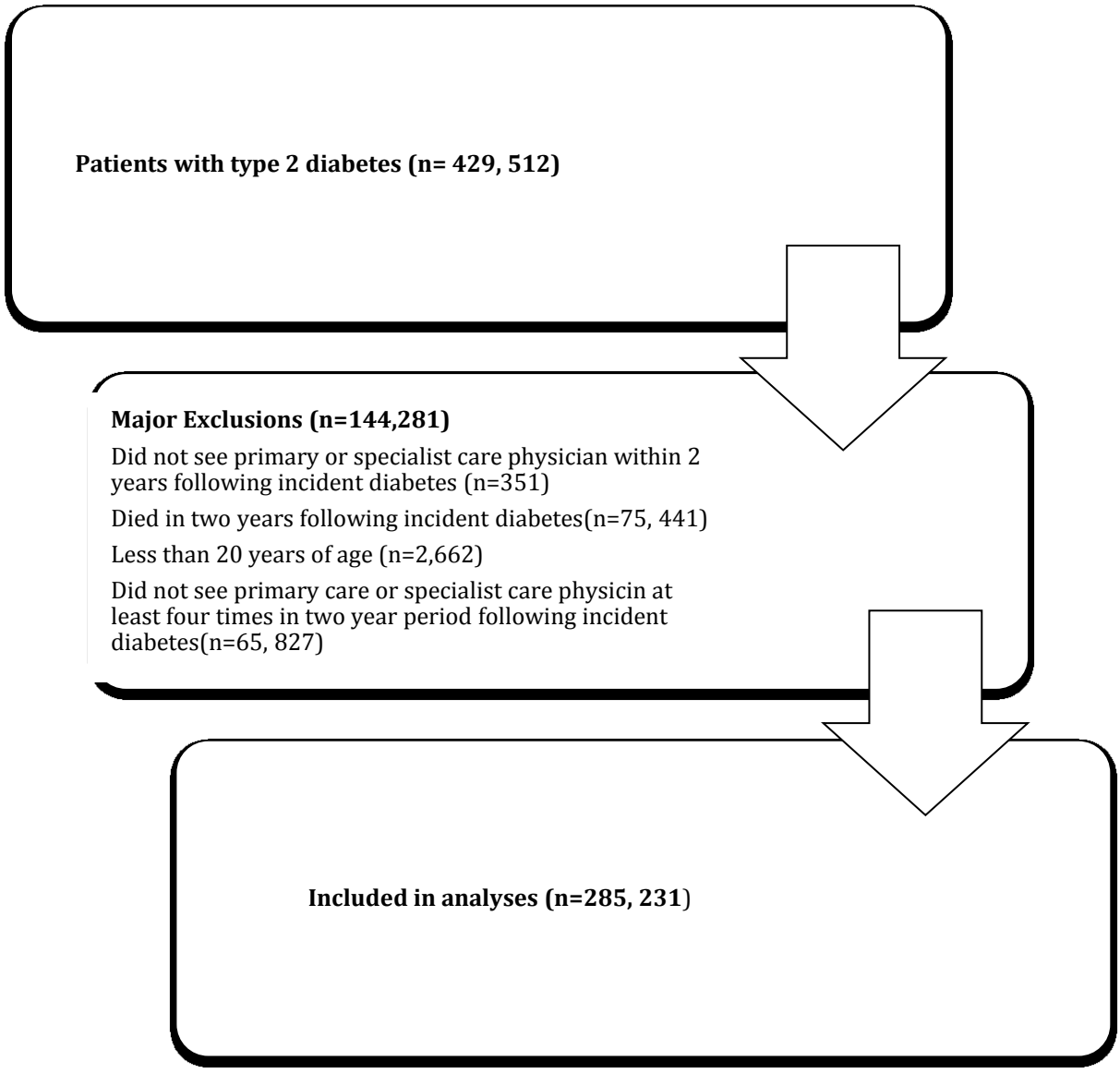


Figure 3-2: Schematic of cohort study design

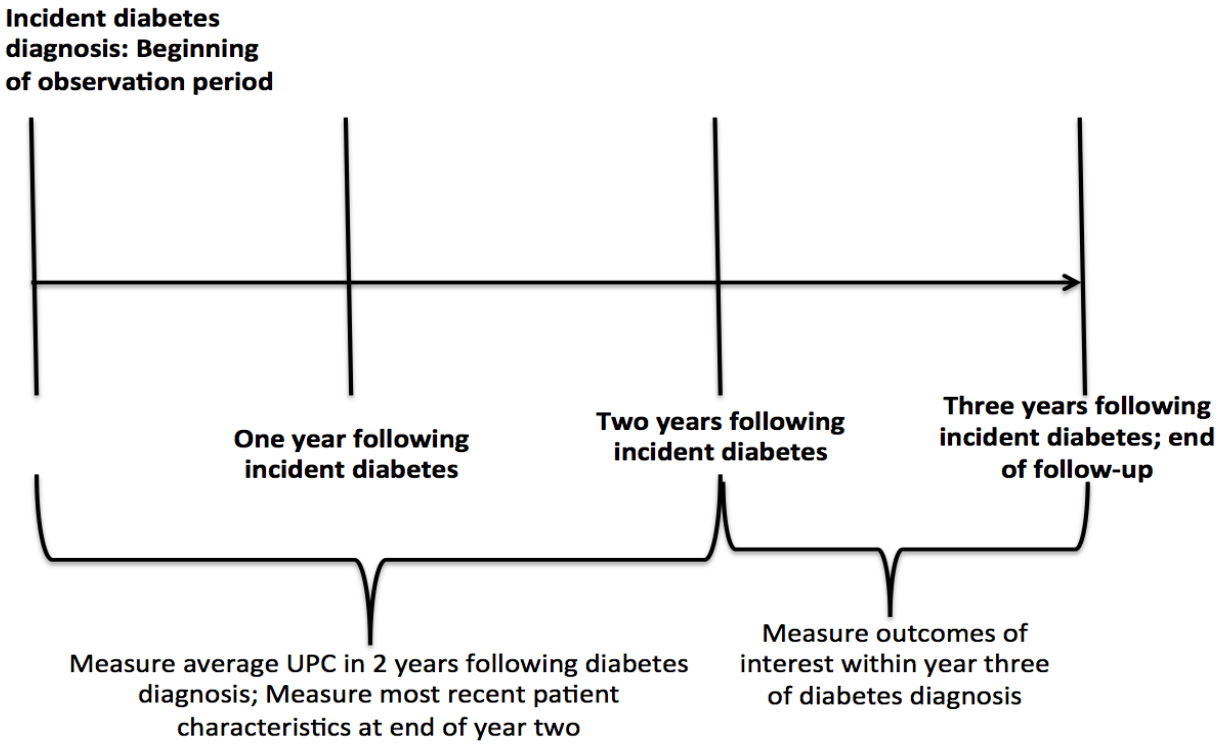
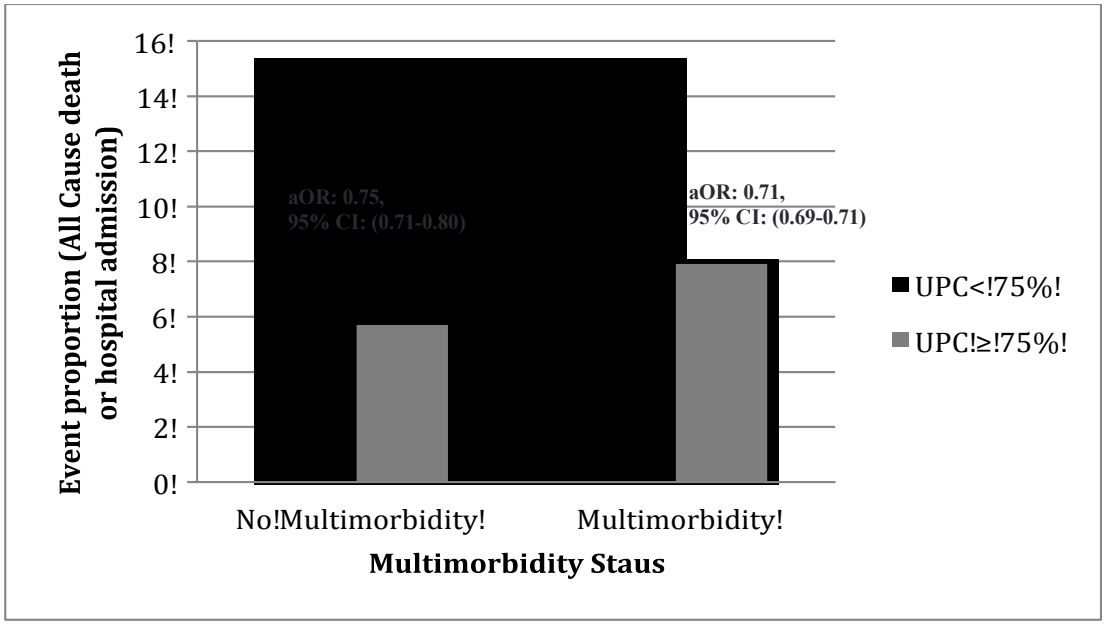


Figure 3-3: All cause death or hospital admission according to provider continuity and multimorbidity status



3.5 References

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CHAPTER 4: SUMMARY

4.1 Summary of Research

The ageing population, continued existence of chronic disease risk factors (including tobacco use, poor nutrition, and low physical activity levels) and improvements in modern medicine all contribute to increasing numbers of individuals with multimorbidity.[1] Thus, the study of these patients is of great importance to improve the health of the overall population moving forward. Patients with multimorbidity are hypothesized to receive suboptimal medical care both during admission for an acute event,[2] as well as in their ongoing day- to- day care.[3] This is posited to be the result of the organization of the acute health care system, in that it is not designed to address the overall health concerns of those with multimorbidity,[4] as well as the fact that those with multimorbidity tend to receive care from multiple providers across a variety of settings, leading to fragmented care.[5] Although a number of studies have evaluated adverse events after an acute event, limited evidence exists as to the contribution of multimorbidity in this setting. Similarly, the effects of continuity of care on health outcomes has been studied in those with chronic diseases such as diabetes,[6] heart failure,[7] and chronic obstructive pulmonary disease (COPD),[8] as well as the elderly (where chronic disease is common).[9] However, the role of multimorbidity in relation to continuity of care has not been adequately addressed.

Our objectives were therefore to determine the extent to which multimorbidity itself has a cumulative effect on risk within an acute care setting as well as the interplay between continuity of care and multimorbidity and its effect on health outcomes. The ultimate aim of this line of research was to help identify high risk patients who may be in need of closer attention within the health system and to inform approaches to management of these high risk patients. These objectives were accomplished by determining the impact of multimorbidity on short-term events in patients with CAP (Chapter 2) as well as evaluating the effect of continuity of care on short-term morbidity and mortality in patients with diabetes both with and without multimorbidity (Chapter 3).

Multimorbidity was common in both of our populations of interest. Although CAP is regarded as an acute event, almost one third of all patients with CAP who visited the emergency department or were admitted to hospital had multimorbidity at the time of the initial event. Furthermore, three quarters of all patients with diabetes had multimorbidity within two years of diabetes diagnosis. Even though it is well known that a chronic disease epidemic is developing worldwide, the substantial clustering of diseases within patients in both the acute and chronic setting is alarming. While the most common chronic conditions in each of the cohorts would be those considered as concordant, or part of the same overall risk profile for each condition of interest, there were also a number of discordant conditions. For example, one of the most common conditions seen in CAP included asthma and COPD which may be expected, however, ischemic heart disease was also common. Similarly, in patients with diabetes, hypertension, angina and cerebrovascular disease were highly prevalent but less expected conditions such as

asthma were also present. Thus, this supports the hypothesis that multimorbidity is often related to the underlying presenting disease continuum in both the acute and chronic diseases setting; however, not all multimorbid disease states are clearly related. As a result, it is important for policymakers as well as clinicians and other healthcare practitioners to take a sufficiently broad viewpoint in the management of patients beyond the presenting disease. Moreover, our results support recent calls for Clinical Practice Guidelines to expand beyond the "silo approach" for disease management and to more broadly incorporate strategies of care better suited for those with multimorbidity. Our results also suggest that a simple count of chronic conditions may be appropriate for defining multimorbidity within certain settings and contexts. Although many more complex measures for multimorbidity exist (such as weighted indices, use of structural equational modelling etc.),[10-12] a more simple measure, similar to the one that we have utilized, is likely to be an important tool for characterizing disease burden for front line clinicians and other healthcare practitioners.

In the acute setting, our results are in line with previous literature suggesting that certain chronic conditions are an important marker of post-discharge outcomes in those with CAP,[13, 14] as we found that multimorbidity in general was associated with an approximately 40% increased risk of death or hospital admission 90-days following discharge from the CAP index event. Although limited data exists, previous literature has demonstrated that the PSI is also a strong predictor of long-term outcomes in CAP patients.[13] Similarly, research has also shown that comorbidities which are part of the PSI such as liver, renal, and cerebrovascular disease, as well as heart failure, can also predict

short-term mortality in those with pneumonia.[15] We have extended this literature to show that a simple count of a wider range of chronic conditions also provides important prognostic information for intermediate-term prediction of adverse events. This clinically important and statistically significant relationship was found even after adjustment for important variables known to have significant impacts on patients with CAP, including functional status. It is important to note that although the PSI alone can predict long-term outcomes, this relationship is likely driven by the underlying chronic conditions a patient has at the time of the initial CAP episode. This is in consideration of the fact that other factors used to calculate the PSI, such as respiratory rate, are unlikely to be directly related to mortality within one year.

The results of our research, as well that of other studies, suggests that both the acute condition itself, as well as comorbid chronic conditions, should be addressed during hospital admissions or ED visits for acute events like CAP. Indeed, multimorbidity is clearly a marker for a sub-population of patients at high risk of adverse events following discharge from acute care. Conversely, it is also likely that multimorbidity has a significant role in triggering the development of the acute health condition in the first place. For instance, studies have suggested that CAP can be the first manifestation of underlying chronic disease, thus potentially indicating those with unrecognized multimorbidity whose health status is severely declining.[15, 16] This suggests that CAP may be a flag in itself for serious comorbidity. Although not specifically addressed in this research, it would seem reasonable to identify high-risk patients with multimorbidity following an acute event for more intensive and active follow-up to mitigate the need for

subsequent hospital admissions or emergency department visits. Moreover, if patients with multimorbidity are receiving effective medical care (i.e., care that is both coordinated and continuous) in the first place, this may too prevent declines in patient health and perhaps prevent the need for future acute care in the first place. However, this would be difficult to evaluate in an acute care setting due to the episodic and often unpredictable pattern of events. It is likely for these reasons, at least in part, that most research evaluating continuity of care to improve health outcomes has been restricted to more "stable" chronic disease states as opposed to those with acute events.

Although a wealth of literature on continuity of care in chronic disease exists, most research in this area has been specific to a single chronic condition with little consideration given to the interplay of continuity of care and multiple chronic diseases within the same patient. Our study, which evaluated the potential role of continuity of care in patients with and without multimorbidity, is one of the first to suggest that reductions in death and hospital admission with continuity of care are similar irrespective of the level of multimorbidity. Continuity of care was associated with an approximate 30% reduction in subsequent death or all-cause hospitalization in patients with diabetes irrespective of multimorbidity status. Although many studies of single chronic diseases have suggested continuity of care is an important mitigating factor for adverse outcomes, most previous literature has been heavily criticized due to the limited control of potentially important factors thought to confound the relationship (e.g., lack of clinical data).[15, 16, 17] In comparison, the methods of our study were reasonably vigorous considering the large number of clinical factors (such as frailty) we were able to adjust

for as well as a number of lab values (such as blood glucose levels) and drug use (including antidiabetic and cardiovascular agents). Moreover, we conducted separate analyses in those with high severity of disease and still found beneficial effects for continuity of care. As multimorbidity is common in patients with diabetes, our results suggest that all patients with diabetes may benefit from better continuity of care. Given the similarity of our results to other studies evaluating a range of chronic conditions, the overall evidence would suggest that continuity of care is important across a wide range of chronic diseases.

Given that continuity of care is clearly important, it is concerning that such a large proportion (approximately 75%) of individuals with diabetes did not have provider continuity. Since the overarching literature has found benefits for continuity of care in a range of populations, and we have demonstrated that continuity of care may be associated with clinically and statistically important reductions in negative health outcomes in those with and without multimorbidity, every effort should be made to improve continuity levels. The best approach for improving continuity of care in patients is uncertain, and likely depends on the nature of a patients disease state. In the case of diabetes, the Canadian Diabetes Association advocates for the 5Rs of care (Recognize, Register, Resource, Relay, and Recall). These guiding principles are targeted at identifying, coordinating and ensuring continuity of care for patients and their providers. This approach would seem reasonable in most chronic disease states, and given the results of our study in CAP, would likely be a reasonable starting point in acute care as well.

4.2 Implications for Future Policy

Our results have many important implications for policy. In general, better policies need to be established around improvements in care for those with multimorbidity, along with greater recognition of improving care for these individuals as a priority area in which to designate health care resources and funding. Although the prevention of chronic disease is more desirable than having to treat chronic disease over a lifetime (both in terms of cost effectiveness and patient health), the avoidance of multiple chronic diseases becomes difficult in older ages despite our best efforts.[17,18] This issue becomes especially important given our ageing population as there is little evidence around the causes and prevention of chronic conditions such as dementia, Alzheimer's, chronic pain and other conditions common in the elderly, therefore, it is an unrealistic expectation to think that the totality of our resources should be spent on the prevention of chronic disease rather than its long-term management.

First, better policies around the coordination of care across acute and long-term care systems need to be established. Among other reasons, this deficiency in coordination may be due to the absence of financial incentives to encourage the continuity and coordination of care activities by physicians.[3] Thus, remuneration systems should be re-designed to reward these practices. Next, policies must be implemented around the development of disease management programs that do not only focus on the treatment of a discrete disease (such as diabetes or chronic kidney disease clinics); rather, they should focus their efforts around management strategies which address the whole patient who

can have multiple chronic conditions. Models such as community health teams may be most effective in meeting this goal. Third, the implementation and effective use of healthcare technologies is also an important area for policy development. The use of technologies such as electronic health records and additional health information exchange platforms could help to facilitate coordinated and continuous care by providing uniform information to all providers caring for an individual with multimorbidity. Policies should also be developed around maximizing the use of proven self-care strategies by those with multiple chronic conditions. Even the highest quality provision of care to individuals with multiple chronic conditions alone will not guarantee improved health outcomes for this population. Individuals must be informed, motivated and involved as partners in their own care. Finally, policies related to follow-up after discharge and discharge planning from hospital or emergency department should also be established. This could include improved post-discharge care plans which recommend home care visits for patients after acute care, as well as follow-up phone calls and other methods of enhanced patient surveillance. These activities all have the potential to reduce the risk of patients being re-admitted to hospital or requiring an ED visit after their initial acute event.

4.3 Implications for Future Research

The results of our studies serve to identify various knowledge gaps in the literature related to multimorbidity. First, it is apparent that more uniform methodologies need to be established to evaluate both multimorbidity and continuity of care. Although these definitions should still be chosen based on the context of the research question under

study, there must be consistencies in the way the concepts are defined as well. Many studies have been conducted related to the effect of continuity of care and multimorbidity on health outcomes separately, and a number systematic reviews have also been published in these subject areas. However, no meta-analyses have been conducted due to significant heterogeneity (largely due to operational definitions) between the included studies for each systematic review; it is nearly impossible to pool any of this data. This leaves only qualitative summaries to describe this body of literature, which are not always suitable.

Next, better identification and implementation of interventions to improve health outcomes in those with multimorbidity should be pursued. Although a recent a systematic review of the literature has already tried to elucidate the relationship between primary care-based interventions and health outcomes in those with multimorbidity, the results were inconclusive.[19] Moreover, the authors acknowledge that it appears to be very difficult to improve health outcomes in this complex population and suggests that targeting risk factors or specific functional difficulties would be the most effective approach.[19] Based on our findings, interventions related to improving continuity of care as well as care within acute settings for those with multimorbidity should be considered.

This also highlights another important area of research related to continuity of care. We have suggested that continuity of care is beneficial, however, this finding is only useful if we are able to develop methods to improve its frequency in the population. We must first

determine patient identified barriers that may be preventing them from having an ongoing relationship with their providers. Based on previous literature, some of these issues could possibly be related to access and socioeconomic status as well as wait times.[20-22] It is also important to identify patient characteristics that may be important predictors of those who are more likely to have continuity of care and those who are not. Through identifying predictors of continuity, those at "high risk" of not having provider continuity could potentially be targeted within the healthcare system.

The external validity/generalizability of clinical trials to those with multimorbidity must also be improved. Historically, patients with multimorbidity have often been excluded from clinical trials and as a result there is little treatment evidence available for these patients. As the number of individuals with multimorbidity grows, ensuring that treatment interventions such as drugs, devices and lifestyle modifications are safe and effective for this group is vital. To achieve this, efforts to improve the understanding of interactions between comorbidities and to limit the exclusion of this increasingly large population in clinical trials must be made. This may include determining the optimal trial design for including patients with multimorbidity, optimizing approaches to recruit patients with multimorbidity and determining the potential risks associated with exposing individuals with multiple chronic conditions to new interventions. Treatment evidence based on clinical trials in those with multimorbidity is likely to assist in preventing adverse events and poor outcomes that otherwise might have occurred. Currently, we wait until treatments or interventions are marketed to the general population where we usually observe unanticipated harms in subgroups of patients, especially the multimorbid

population. Initial inclusion of these patients in trials, therefore, may mitigate the impact of harms on the larger population of interest.

The pursuit of these potential areas of research would all serve to help develop clinical practice guidelines for those with multimorbidity. The lack of guidelines for the treatment of this population has long been cited as one of the largest barriers to providing effective medical care to these patients.[23, 24] Although the need for individualized and patient centred care is especially important in those with multimorbidity, physicians still require better tools in order to make care decisions. Indeed, it has been suggested that the way we approach clinical targets such as blood glucose and blood pressure levels as well as treatment with pharmacologic agents should be modified from what is currently presented in guidelines for those with multimorbidity.[25, 26] These treatment options and care decisions should always be made in the context of patient preferences. For example, although clinical practice guidelines suggest that patients with diabetes who do not meet blood glucose targets should also be initiated on a second oral agent or injectable medication, this may not be appropriate if the patient also has heart failure.[27] For this particular patient, controlling blood pressure levels might be more beneficial for their care, therefore, physicians may less aggressively treat blood glucose levels with anti-diabetic agents. This treatment choice would be left up to the discretion of the patient and their physician, however, it would likely be beneficial if these types of treatment choices were also outlined within clinical practice guidelines to help guide the clinical decision making process.

4.4 References

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