The Association of Diabetes with Frequency and Cost of Hospital Admissions

Journal:	*CMAJ*
Manuscript ID	CMAJ-19-1531
Manuscript Type:	Research - Cohort study (retrospective)
Date Submitted by the Author:	13-Nov-2019
Complete List of Authors:	Choi, Hyoungjin; University of Toronto, Medicine Booth, Gillian; St. Michael's Hospital, Centre for Urban Health Solutions Verma, Amol; St. Michael's Hospital, Li Ka Shing Centre for Healthcare Analytics Research and Training; University of Toronto, Medicine Jung, Hae Young; Li Ka Shing Knowledge Institute Lapointe-Shaw, Lauren; University Health Network, Division of General Internal Medicine Tang, Terence; Trillium Health Partners, Program of Medicine and Institute for Better Health Kwan, Janice; Mount Sinai Hospital, Department of Medicine Rawal, Shail; University Health Network, Division of General Internal Medicine Weinerman, Adina; Sunnybrook Health Sciences Centre, Division of General Internal Medicine Razak, Fahad; Li Ka Shing Knowledge Institute; St Michael's Hospital, Division of General Internal Medicine
More Detailed Keywords:	diabetes, epidemiology, hospitalization, cost, prevalence
Keywords:	Diabetes, Epidemiology
Abstract:	Background: Acute inpatient hospitalizations account for greater than half of all healthcare costs related to diabetes. We identified the frequency and costs of the most common conditions leading to hospitalization among patients with diabetes, compared to patients without diabetes. Methods: We used data from a retrospective cohort study of all General Internal Medicine patients in seven Toronto hospitals between 2010 and 2015. The Canadian Institute for Health Information (CIHI) Most Responsible Diagnosis code was used to identify the ten most frequent reasons for admission in patients with diabetes. Cost of hospitalization was estimated using the CIHI Resource Intensity Weight. Comparisons were made between patients with or without diabetes using Pearson's $\chi 2$ test for frequency and distribution-free confidence intervals for median cost. Results: Among the 148,388 hospitalizations in our study, 28% involved patients with diabetes. Compared to patients without diabetes, hospitalizations due to soft tissue and bone infections were most frequent (2.5% vs. 2.0%; prevalence ratio [PR] 1.27, 95% confidence interval [CI] 1.18-1.37) and costly (CAD $8,795 vs. CAD $5,845; cost

	ratio [CR] 1.50, 95%CI 1.37-1.65) among patients with diabetes. This was followed by urinary tract infections (PR 1.15, 95%CI 1.10-1.21, CR 1.23, 95%CI 1.17-1.29), stroke (PR 1.13, 95%CI 1.07-1.19, CR 1.19, 95%CI 1.14-1.25), and electrolyte disorders (PR 1.11, 95%CI 1.03-1.19, CR 1.20, 95%CI 1.08-1.34). Interpretation: Soft tissue and bone infections, urinary tract infections, stroke, and electrolyte disorders are associated with a greater frequency and cost of hospitalization in patients with diabetes than in those without diabetes.

THE ASSOCIATION OF DIABETES WITH FREQUENCY AND COST OF HOSPITAL ADMISSIONS

Jin Choi[1] MD MSc, Gillian Booth[2,3] MD MSc, Amol Verma[2,4] MD MPhil, Hae Young Jung[2] MSc, Lauren Lapointe-Shaw[5] MD PhD, Terence Tang[6] MD, Janice L. Kwan[7] MD MPH, Shail Rawal[5] MD MPH, Adina Weinerman[8] MD MHSc, and Fahad Razak[2,4] MD MSc

Department of Medicine, University of Toronto[1];
Li Ka Shing Knowledge Institute, St. Michael's Hospital[2];
Division of Endocrinology, St. Michael's Hospital[3];
Division of General Internal Medicine, St. Michael's Hospital[4];
Division of General Internal Medicine, University Health Network[5];
Program of Medicine and Institute for Better Health, Trillium Health Partners[6];
Division of General Internal Medicine, Mount Sinai Hospital[7];
Division of General Internal Medicine, Sunnybrook Health Sciences Centre[8];
Toronto, Ontario, Canada

Correspondence to:
Fahad Razak, Fahad.Razak@unityhealth.to, 416-864-6060 ext. 77430

Funding statement:
The General Internal Medicine Inpatient Initiative (GEMINI) study was supported by grants from Green Shield Canada Foundation and the Division of General Internal Medicine, University of Toronto. F.R. is supported by an award from the Mak Pak Chiu and Mak-Soo Lai Hing Chair in General Internal Medicine, University of Toronto.

Conflicts of interest:
A.V. and F.R. report that they are part-time employees of Health Quality Ontario, the Provincial Clinical Lead for Quality Improvement in General Internal Medicine. No other competing interests were declared.

ABSTRACT

Background: Acute inpatient hospitalizations account for greater than half of all healthcare costs related to diabetes. We identified the frequency and costs of the most common conditions leading to hospitalization among patients with diabetes, compared to patients without diabetes.

Methods: We used data from a retrospective cohort study of all General Internal Medicine patients in seven Toronto hospitals between 2010 and 2015. The Canadian Institute for Health Information (CIHI) *Most Responsible Diagnosis* code was used to identify the ten most frequent reasons for admission in patients with diabetes. Cost of hospitalization was estimated using the CIHI *Resource Intensity Weight*. Comparisons were made between patients with or without diabetes using Pearson's χ^2 test for frequency and distribution-free confidence intervals for median cost.

Results: Among the 148,388 hospitalizations in our study, 28% involved patients with diabetes. Compared to patients without diabetes, hospitalizations due to soft tissue and bone infections were most frequent (2.5% vs. 2.0%; prevalence ratio [PR] 1.27, 95% confidence interval [CI] 1.18-1.37) and costly (CAD $8,795 vs. CAD $5,845; cost ratio [CR] 1.50, 95%CI 1.37-1.65) among patients with diabetes. This was followed by urinary tract infections (PR 1.15, 95%CI 1.10-1.21, CR 1.23, 95%CI 1.17-1.29), stroke (PR 1.13, 95%CI 1.07-1.19, CR 1.19, 95%CI 1.14-1.25), and electrolyte disorders (PR 1.11, 95%CI 1.03-1.19, CR 1.20, 95%CI 1.08-1.34).

Interpretation: Soft tissue and bone infections, urinary tract infections, stroke, and electrolyte disorders are associated with a greater frequency and cost of hospitalization in patients with diabetes than in those without diabetes.

INTRODUCTION

Diabetes inflicts a heavy burden on health care systems globally.[1] In Canada and the US, nearly one in ten people are diagnosed with diabetes,[2,3] and this figure has been projected to increase to one in five people by 2050.[4] In 2008, diabetes cost Canada $2.18 billion in the form of hospitalizations, physician care, and medications.[5] By 2022, new cases of diabetes have been estimated to cost an additional $15.36 billion.[6] In the US, a quarter of all US health care expenditures in 2017 were incurred by people with diabetes.[3]

Acute inpatient hospitalizations are the primary driver of healthcare costs related to diabetes in Canada and the US. In many jurisdictions including Ontario, Canada, greater than 50% of attributable costs in incident diabetes are accounted by acute inpatient hospitalizations.[3,7] Research has shown diabetes to portend a higher likelihood of heart failure,[8] stroke,[9] and renal failure[10] separately. However, there is a paucity of data describing the specific medical conditions that drive the increased frequency and cost of hospitalization among people with diabetes. Such population-level data could specifically guide public policy in strengthening support for greater outpatient services among people with diabetes.

The objectives of this study are to identify the frequency and costs of the most common conditions leading to hospitalization among patients with diabetes, compared to patients without diabetes.

METHODS

Study Design and Population

This is a retrospective cohort study using data collected by the General Internal Medicine Inpatient Initiative (GEMINI) study, which involves 7 large hospital sites affiliated with the University of Toronto. This study included all patients admitted to or discharged from the General Internal Medicine service at each hospital between April 1, 2010 and March 31, 2015. This includes patients cared for by General Internal Medicine who required an Intensive Care Unit (ICU) admission at any point during their hospitalization or who were transferred to surgical services (for example, for an amputation). There were no exclusion criteria.

A full description of the design and methods of GEMINI has been previously presented.[11] General Internal Medicine accounted for a significant proportion of hospitalizations, including 39% of all emergency admissions. The most responsible care providers on the General Internal Medicine wards were predominantly Internists. A separate inpatient cardiology ward was ubiquitous among all hospitals, but access to respirology, nephrology, hematology, gastroenterology, oncology, and stroke wards varied. There were no separate endocrinology inpatient wards at any centres.

Data collection

We collected patient-level characteristics for each admission, including demographic characteristics, diagnoses, interventions, discharge destination and resource use as reported by participating hospitals to the Canadian Institute for Health Information (CIHI) Discharge Abstract Database. Patients with diabetes were identified using CIHI Diagnosis Code (Group 10,

Field 02) which conveys International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) codes as recorded in hospital administrative databases.

For each admission, we identified the primary discharge diagnosis using ICD-10 codes. Diseases were then classified into clinically relevant categories using the Clinical Classifications Software (CCS) tool, which aggregates individual diagnoses into 285 mutually exclusive categories.[11]

To estimate the cost of each hospitalization comparably across sites and years, we used the CIHI Resource Intensity Weight for each admission using the 2015 grouping methodology[12] and multiplied this by the annual cost per weighted case for acute inpatient cases that was reported for each hospital using the Ontario Cost Distribution Methodology.[13] This approach estimates the average amount of hospital resources used for each hospital stay, including costs related to administration, staff, supplies, technology, and equipment, but does not include fee-for-service physician billing costs. Data from the CIHI has been previously validated[14,15] and reliably formed the basis for a substantial body of clinical and health services research.[16,17]

In order to compare the absolute burden and cost of care between individuals with and without diabetes, unadjusted rather than adjusted costs were reported. All costs were reported in Canadian Dollars (CAD).

Ethics

Research Ethics Board approval was obtained from all participating hospitals. Waivers of informed consent were obtained because this was a large retrospective study with minimal risk of re-identification for any individual patient.

Statistical analysis

The study population was described using means and standard deviations (SD) or medians and interquartile ranges (IQR), as appropriate for continuous or interval distributions, and frequencies for categorical variables. Comparisons were made between patients with or without diabetes using Pearson's χ^2 test for frequency and distribution-free confidence intervals for median cost. Our cost data did not satisfy the traditional Mann-Whitney assumption that the distributions of comparison groups are identical to test for the equal medians, thus we employed an alternative distribution-free confidence interval method to compare median costs in our study.[18] For the top ten most frequent reasons for admission among patients with diabetes, we compared frequency and cost of admission using prevalence ratios and cost ratios. Prevalence and cost ratios were computed as the ratio of frequency or cost in patients with diabetes to the frequency or cost in patients without diabetes.[19] Given large sample sizes, we determined differences to be meaningful if they were both statistically significant and ratios were greater than a 10% difference. Cohen[20] has classified an effect size for prevalence comparisons as being small if <20%, and we a priori set an even smaller threshold of a 10% difference to err on the side of over-inclusiveness when trying to identify meaningful differences in cost and prevalence between people with or without diabetes. Further, we conducted sensitivity analyses using only the first hospitalization for all included patients. All analyses were conducted using the R statistical package, version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study population

There were 148,388 admissions to General Internal Medicine across all hospital sites during the study period. There were 96,073 unique patients. Overall, 41,464 (28%) of all hospitalizations occurred in patients with diabetes, and the majority of hospitalizations (94%) were among patients with type 2 diabetes. Among all hospitalized patients, the median age was 73 years, 50.3% were female, and the mean number of comorbidities was 6.

Frequency of admissions

The most frequent reasons for admission to General Internal Medicine (Table 1, Table 2) among patients with diabetes were heart failure (7.8%), urinary tract infection (5.1%), stroke (4.8%), pneumonia (4.6%), chronic obstructive pulmonary disease (4.5%), delirium (3.2%), acute renal failure (2.9%), sepsis (2.7%), soft tissue and bone infections (2.5%), and electrolyte disorders (2.4%). In the CCS group of electrolyte disorders, the most common were hyponatremia (57%), dehydration (14%), hypernatremia (10%), hyperkalemia (6%), and hypokalemia (4%) (Data not shown).

The prevalence ratios for these conditions (Figure 1) showed that acute renal failure (prevalence ratio [PR] 2.02; 95% confidence interval [CI] 1.87-2.18), heart failure (PR 1.87; 95%CI 1.79-1.96), soft tissue and bone infections (PR 1.27; 95%CI 1.18-1.37), sepsis (PR 1.27; 95%CI 1.18-1.36), urinary tract infections (PR 1.15; 95% CI 1.10-1.21), delirium (PR 1.15; 95% CI 1.08-1.23), stroke (PR 1.13; 95%CI 1.07-1.19), and electrolyte disorders (PR 1.11; 95%CI 1.03-1.19) were more common reasons for hospitalization among patients with diabetes compared to those without.

Cost of admissions

The median cost of admission (Table 1) for each of the most common reasons for admission among patients with diabetes were $6,812 for heart failure, $5,442 for urinary tract infection, $8,270 for stroke, $6,183 for pneumonia, $6,278 for chronic obstructive pulmonary disease, $12,952 for delirium, $6,301 for acute renal failure, $10,487 for sepsis, $8,795 for soft tissue and bone infections, and $4,422 for electrolyte disorders.

The cost ratios for these conditions (Figure 2, Table 2) showed that admission for soft tissue and bone infections (cost ratio [CR] 1.50, 95%CI 1.37-1.65), urinary tract infection (CR 1.23, 95%CI 1.17-1.29), electrolyte disorders (CR 1.20, 95%CI 1.08-1.34), and stroke (CR 1.19, 95%CI 1.14-1.25) were more costly among patients with diabetes compared to those without. The proportional difference in cost of admission for heart failure, pneumonia, and chronic obstructive pulmonary disease were statistically significant but were not greater than our threshold of 10%.

Sensitivity analyses

Sensitivity analyses that used only the first hospitalization for each patient (n=96,073) did not significantly change our results.

INTERPRETATION

In our study of General Internal Medicine patients, nearly a third had diabetes. Soft tissue and bone infections, urinary tract infections, stroke, and electrolyte disorders were more frequent and costly among patients with diabetes compared to patients without. In addition, hospitalizations for acute renal failure, heart failure, sepsis, and delirium occurred at a greater frequency in the diabetes population, but not at an increased cost.

Diabetes is a highly prevalent and potential driver of illness among hospitalized patients. A recent study has found hypertension to be the most common comorbid condition among patients admitted to hospital with diabetes as the primary admitting reason.[21] However as we have demonstrated, diabetes is rarely itself a reason for admission, but more frequently leads to morbidity and subsequent hospitalization through its multiple potential complications including soft tissue and bone infections, urinary tract infections, stroke, and electrolyte disorders. To our knowledge, our study is the first to provide this essential information for clinicians and policy-makers to understand the broader impact of diabetes on hospitalizations.

Our findings on stroke add to existing knowledge: patients with diabetes have approximately twice the risk of stroke compared with those without diabetes.[22] Rates of stroke have fallen substantially over the last few decades in response to the growing evidence in support of cardioprotective therapies and their adoption to clinical practice.[23] Yet, based on our evidence, admissions for stroke remain more common in patients with diabetes.

In comparison to stroke, the prevention of soft tissue and bone infections have received less attention in the research literature, potentially at the expense of increased morbidity and mortality.[24] In Canada and the US, decades of improvements in rates of non-traumatic lower

extremity amputations in patients with diabetes have recently reversed, especially among younger adults.[25,26] A 2017 international meta-analysis comparing the prevalence of diabetic foot ulcers across 33 countries has found Canada (14.8%) to have the second highest rate, after Belgium (16.6%).[27] Foot care is one of the most neglected components of standard diabetes care practices, with only 51% of Canadian patients with diabetes having their feet checked as recommended.[28] With the exception of recent coverage in Ontario, Canada, offloading devices are not currently covered for Canadians with diabetes suffering from foot ulcers.[29] In addition, the prevalence of diabetes is higher in lower-income households,[30] providing real-life context to the 57% of Canadians with diabetes who cannot afford their necessary medications, devices, and supplies.[31]

In order to curb such trends in soft tissue and bone infections, proven preventive modalities including regular foot examination, debridement, mechanical offloading devices, and chiropody must not only be available, but approachable and easily accessible for patients with diabetes who often lack economic or social capital. As part of increasing efforts to integrate information technology into medicine,[32] the recruitment of telemedicine[33] and social media[34] in diabetes foot care may help fill in gaps in accessibility and knowledge dissemination. Given the projected increase in the burden of diabetic foot ulcers, including frequent and costly admissions to hospital as shown in our study, increased primary care efforts and public funding should be specifically directed towards proven preventive strategies and modernized approaches.[35]

Most of our identified diabetes-related conditions were vascular in nature, except for urinary tract infections, delirium and electrolyte disorders. The increased burden of hospitalization secondary to urinary tract infections in diabetes is consistent with existing knowledge.[36] Diabetes is associated with a higher risk of asymptomatic bacteriuria, urinary tract

infections, and severe complications. Whether patients with diabetes should be treated if they have asymptomatic bacteriuria is unknown and may be an important focus of future research. In addition, ongoing review of the safety of sodium-glucose cotransporter-2 (SGLT2) inhibitors, which are gaining prominence in diabetes care, is needed to understand its impact on urinary tract infections among patients with diabetes.[37]

Although delirium may be caused by any one of the identified conditions, there is limited literature on how diabetes can predispose an individual to delirium directly. Diabetes has been associated with both Alzheimer's and vascular dementia,[38] yet studies on its association with delirium has been yielded mixed results, and primarily conducted in an intensive care setting.[39] One plausible hypothesis is the generation of microvascular malformations in the central nervous system from persistent metabolic derangements leading to endothelial damage and deregulated angiogenesis.[40] Given that the prevalence of delirium among our patients with diabetes was 24% higher than among those without, further studies are warranted to understand the mechanism behind this increased prevalence.

Electrolyte disorders were one of the most frequent and costly reasons for admission in patients with diabetes, yet preventive strategies are lacking. The multifactorial nature of its pathophysiology in diabetes, likely including poor nutrition, impaired gastrointestinal absorption, acid-base abnormalities, and pharmacological agents make electrolyte abnormalities a challenging condition to prevent.[41] Further studies that aim to elucidate the individual pathophysiologic mechanisms of electrolyte disorders in patients with diabetes will be necessary in developing outpatient strategies for monitoring and prevention.

Limitations

There are several limitations to our study. First, our patients with diabetes were restricted to those who were admitted for some portion of their hospitalization under a General Internal Medicine service, and not surgical, psychiatric, or subspecialty medical services. Thus, the frequency of admissions secondary to diabetes-related complications may be underestimated for conditions (e.g. acute coronary syndrome) where admissions may occur to non-General Internal Medicine services. In addition, patients with severe complications may be admitted to a non-medical service, such as those with osteomyelitis under Orthopaedics. However, General Internal Medicine now represents more than a third of all emergency room admissions to hospital and therefore our data captures the largest group of patients requiring hospitalization and represents a crucial health services group on which to focus.[11] Second, our cost estimations do not take physician billing and outpatient expenses into account. This would lead to underestimations of cost of admission and this may affect the cost ratio methods we adopted. Third, our use of the RIW provides an estimation to the cost of hospital admission but not out-of-pocket costs including mechanical offloading devices. However, RIW has been previously used in similar studies,[7,42] and provides a reasonable estimation for the direct healthcare costs attributable to diabetes. Fourth, our patient population encompasses only two cities in Canada. However, our inclusion of the five largest hospitals in Toronto and the only two hospitals in Mississauga, Canada's first and ninth most populous municipalities respectively, adds to our generalizability.

Conclusion

There is a substantial burden of diabetes on acute hospitalizations. This is the first study to characterize the frequency and costs associated with acute inpatient hospitalizations from various diabetes-related conditions in General Internal Medicine. Based on our findings, a preventive strategy focused on reducing hospitalizations secondary to soft tissue and bone infections,

urinary tract infections, stroke, and electrolyte disorders in patients with diabetes may be beneficial in this high-risk group.

ACKNOWLEDGEMENTS

J.C. wrote the first draft of the manuscript. H.Y.J. provided statistical analysis. J.C., G.B., A.V., F.R. contributed to the interpretation of data, critically revised the manuscript, and approved the final version for submission. L.L.S., T.T., J.K., S.R., and A.W. critically revised the manuscript. F.R. is the guarantor of this work and as such, had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis.

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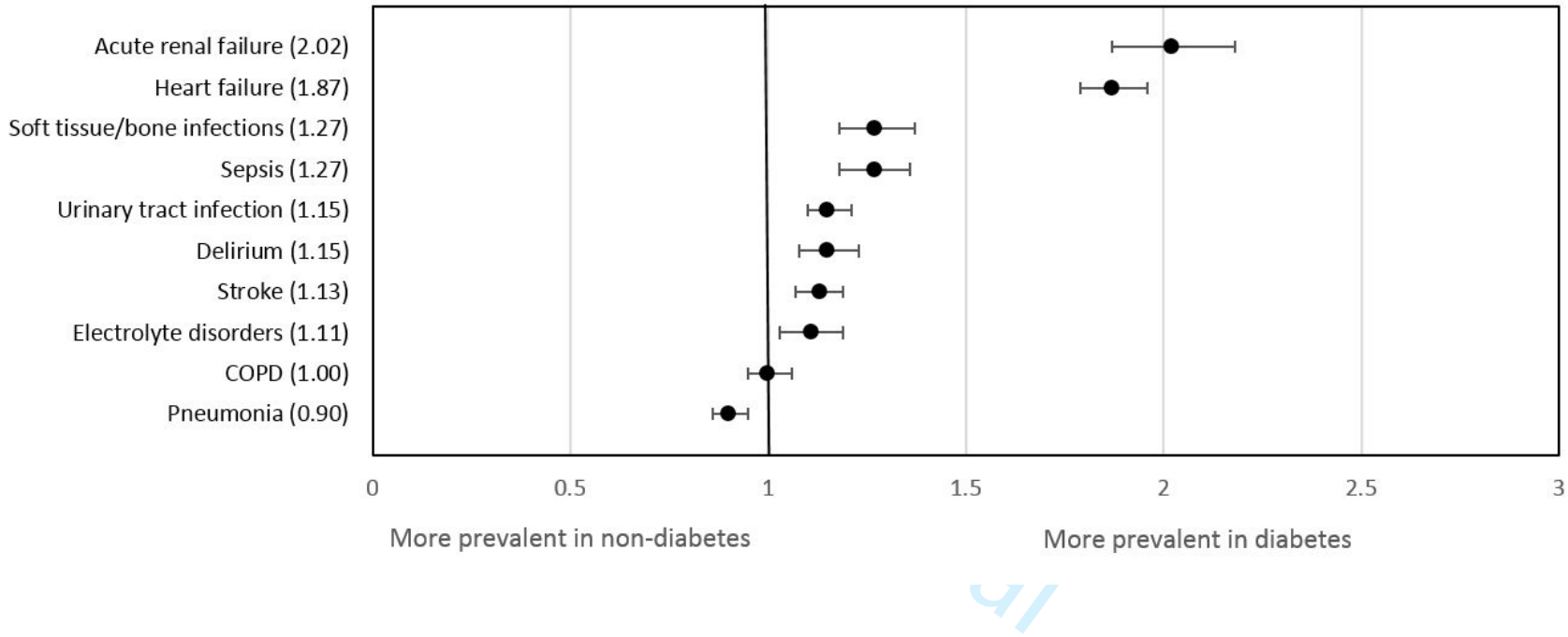
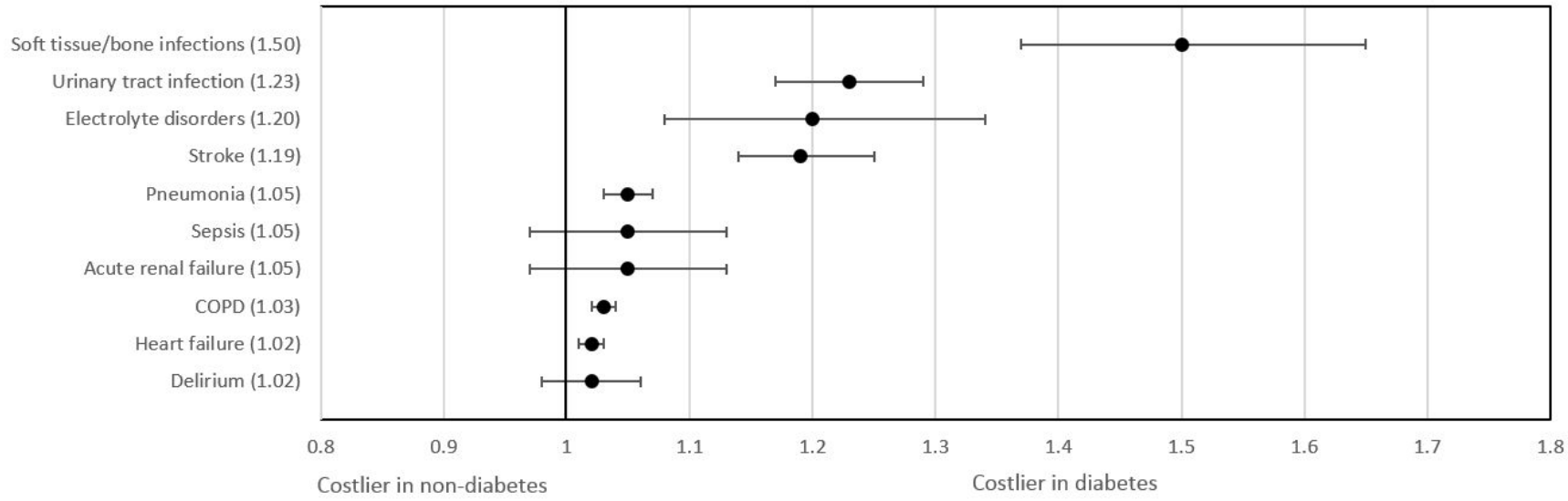
Figure 1. Prevalence ratios of most responsible reasons for diagnosis



Most responsible diagnosis (prevalence ratio).

Figure 2. Cost ratios of most responsible reasons for diagnosis



Most responsible diagnosis (cost ratio).

Table 1. Prevalence and cost of admission for most common reasons for hospitalization, stratified by diabetes status

Most Common Reason for Hospitalization	Prevalence, N (%)			Cost of Admission, median (CAD)		
	Overall	Diabetes	No Diabetes	Overall	Diabetes	No Diabetes
Heart Failure	7639 (5.1)	3215 (7.8)	4424 (4.1)	6717	6812	6670
Urinary tract infection	6890 (4.6)	2129 (5.1)	4761 (4.5)	5071	5442	4427
Cerebral infarction	6556 (4.4)	1996 (4.8)	4560 (4.3)	7122	8270	6922
Pneumonia	7381 (5.0)	1914 (4.6)	5467 (5.1)	6010	6183	5902
COPD	6605 (4.5)	1848 (4.5)	4757 (4.4)	6148	6278	6095
Delirium	4345 (2.9)	1342 (3.2)	3003 (2.8)	12831	12952	12700
Acute renal failure	2726 (1.8)	1197 (2.9)	1529 (1.4)	6176	6301	6025
Sepsis	3434 (2.3)	1132 (2.7)	2302 (2.2)	10025	10487	9995
Soft tissue and bone infections	3127 (2.1)	1032 (2.5)	2095 (2.0)	6721	8795	5845
Electrolyte disorders	3365 (2.3)	1010 (2.4)	2355 (2.2)	3768	4422	3679

COPD (Chronic Obstructive Pulmonary Disease). CAD (Canadian Dollars).

Table rows ordered by prevalence among people with diabetes.

Table 2. Most Common Reasons for Hospitalization, stratified by increase in prevalence and cost of hospitalization

		Cost of Admission in Diabetes	
		Increased*	Not Increased
Prevalence of Admission in Diabetes	Increased*	Stroke Urinary tract infection Soft tissue/bone infections Electrolyte disorders	Acute renal failure Heart failure Sepsis Delirium
	Not Increased		Pneumonia COPD

COPD (Chronic Obstructive Pulmonary Disease).

**Both statistically significant and greater than 10% increase.*