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Risk Factors and Direct Medical Cost of Early versus Late Unplanned Readmissions among Diabetes Patients at a Tertiary Hospital in Singapore

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ABSTRACT

Objective: To examine the risk factors and direct medical cost associated with early (≤30 days) versus late (31-180 days) unplanned readmissions among patients with type 2 diabetes in Singapore.

Methods: Risk factors and its associated cost among diabetes patients were investigated using electronic medical records from a local tertiary care hospital from 2010 to 2012. Multivariable logistic regression was used to identify risk factors associated with early and late unplanned readmissions while generalized linear model was used to estimate the direct medical cost. Sensitivity analysis was also performed.

Results: 1,729 diabetes patients had unplanned readmissions within 180 days of an index discharge. Length of index stay (a marker of acute illness burden) was one of the risk factors associated with early unplanned readmission while patient behavior-related factor like the diabetes-related medication adherence was one of the factors associated with late unplanned readmission. Adjusted mean cost of index admission was higher among patients with unplanned readmission. Sensitivity analysis yield similar results.

Conclusions: Existing routinely-captured data can be used to develop prediction models that flag out high risk patients during their index admission; potentially helping to support clinical decisions and prevent such readmissions.

Keywords: readmission; unplanned; diabetes; cost; risk factor

INTRODUCTION

Unplanned hospital readmissions are costly yet usually preventable [1]. A study has shown that unplanned readmissions cost US$17.4 billion in 2004, accounting for 17.0% of hospital payments from Medicare in the U.S. [2]. Reducing hospital readmission rates was one of the World Health Organization's top strategic priorities in 2005 as controlling unnecessary hospital readmissions not only reduces wasteful spending but improves patients' quality of life [3].

Singapore has the second highest prevalence of diabetes patients in the developed countries (11.3% in 2010) and diabetes is a common primary or comorbid condition among patients who readmit [4,5]. However, to the best of our knowledge, only one study of early and late (after 30 days of discharge) readmissions examined diabetes mellitus as one of the primary conditions of interest [6] but treated diabetes as a risk factor while most similar research focused on early readmissions (within 30 days of discharge) only [7,8]. As several studies have reported a substantial proportion of patients who experienced late readmissions [9–14], exclusion of late readmissions in the analysis could understate the true burden of readmissions.

Risk factors associated with early and late readmissions have been suggested to differ, as early readmission was said to be associated with acute illness burden while the latter was associated with chronic illness burden [15]. However, there is difficulty comparing readmissions across studies due to a lack of standardized definition particularly in terms of the type of readmission, duration of follow-up and planned versus unplanned readmissions [8]. Some studies defined readmissions as an inpatient-to-inpatient event which will result in a large source of missing potentially preventable healthcare utilization managed solely by the Emergency Department. Next, early readmissions could be defined between 7 to 30 days [8,15] after discharge while late readmissions could be defined as any hospitalization within 8 to 365 days [15,16] after initial discharge from the hospital.

Furthermore, these studies are usually limited to the elderly population (65 years old and above) [6,17]; do not examine medication issues although medication management is an important component of discharge planning and transitional care for diabetes patients [18]; or estimate the cost associated with such readmissions. Therefore, this study aims to examine the risk factors associated with early and late unplanned readmissions via an exploratory descriptive analysis among adult type 2 diabetes patients and estimate the costs associated with these admissions.

METHODS

Database and study population

A cross-sectional study was conducted using electronic medical records (EMRs) from a 1000-bed academic tertiary care hospital in Singapore from January 2010 to January 2012. This study was approved by the National Healthcare Group Domain Specific Review Board (Protocol No.: 2011/00090). Waiver of consent was also approved as the research involved no more than minimal risk to the subjects.

Adult type 2 diabetes patients, who are citizens or permanent residents of Singapore aged 21 years old and above, were identified from the merged database by the presence of ICD-9-CM codes (250.x0 or 250.x2) or an ICD-10-AM code for type 2 diabetes (E11.x) from 1 July 2010 – 1 July 2011. Alternatively, patients without the aforementioned criteria were included if they had at least one anti-diabetic medication (insulin or oral hypoglycemic agents) dispensed during their outpatient or inpatient visit, which is similar to the algorithm used to identify diabetes patients in the local National Healthcare Group Chronic Disease Management System [19]. This is because patients would likely not have a clinical diagnosis for diabetes captured in the database if they did not visit the hospital for diabetes-related medical issues since it is not a requirement to record all relevant ICD codes during each visit. As the studied population is type 2 diabetes (which constitutes 80% of all diabetes cases in Singapore [20]), other types of diabetes (namely type 1 diabetes and gestational diabetes) were excluded from this study. In addition, other than excluding episodes with missing data, cases were also excluded if they died during the index admission or if they had an index admission within 180 days of a previous hospitalization discharge before 1 July 2010, such that the index admission studied would be a readmission of a previous hospital stay if included. This resulted in only one index admission per patient being considered in this study due to its short time horizon.

Outcomes

The primary outcomes of the study are early unplanned readmissions and late unplanned readmissions, defined as an emergency admission within 30 days and within 31-180 days of discharge from the index admission respectively. Index admission refers to the first admission (excludes day surgery) that occurred within the study period from 1 July 2010 to 1 July 2011. Secondary outcomes include direct medical costs associated with index admission and readmission.

Independent variables

A literature review was conducted to identify risk factors that were significantly associated with readmission among diabetes patients (refer to Appendix 1 of the Supplemental materials). General models of readmission (e.g. LACE model [21] which has been validated in the Singapore population) were not investigated as diabetes would be treated as a risk factor of readmission (often included as part of a comorbidity burden score). The identified risk factors that were available in the EMRs during the patients' index admission and relevant to the Singapore healthcare setting were included in this study.

These variables consisted of gender, ethnicity, age (21-64 years old or 65 years old and above because elderly patients are more likely to readmit [22]), whether the patient was discharged against medical advice, whether the index admission was planned or unplanned such that patients who were admitted via the emergency department were categorized as 'unplanned', length of index stay, primary reason for index admission (which is characterized using ambulatory care sensitive conditions (ACSCs)), severity of diabetes-related complications (measured using Diabetes Complications Severity Index (DCSI)), burden of comorbidities (measured using Elixhauser comorbidities (ECs), diabetes-related drug modification, and their HbA1c level. Other than the risk factors identified from the literature review, adherence to diabetes-related medication (measured using the average proportion of days covered (PDC)) which has not been analyzed before with unplanned readmission among diabetes patients was included in this study. Detailed description of the independent variables is available in Appendix 2 of the Supplemental materials.

All the clinical conditions in the ACSC, DCSI and comorbidities were identified using both ICD-9 and ICD-10 codes [23] except for lower extremity amputation because ICD-10 Procedure Coding System (ICD-10-PCS) codes were not available in our database. The ICD-10-AM procedure code, an alternative to ICD-10-PCS codes, was not used as an equivalence mapping tool was not available.

Cost assessment

Direct medical costs associated with readmissions included diabetes-related costs such as clinical services, consumables, drugs and laboratory services directly attributable to the consumption of health services incurred within the hospital. All costs here are from the health system perspective and expressed in U.S. dollars according to the year the services were consumed (2010: 1 USD=1.36 SGD, 2011: 1 USD=1.26 SGD, 2012: 1 USD=1.25 SGD) [24,25].

Statistical analysis

All statistical analyses were two-sided with significance level set at 5% and computed using STATA version 13.1 (StataCorp, College Station, Texas, U.S.). Categorical variables were presented as counts and proportions and compared using Pearson's chi-square test. Continuous variables were presented in median with the 25th and 75th percentiles and compared using the Wilcoxon-Mann-Whitney test for an independent variable with two groups and the Kruskal-Wallis test for three groups. A Dunn test with Bonferroni correction was performed for multiple pairwise comparisons among three groups.

Multivariable logistic regressions were used to assess the influence of risk factors on early and late unplanned readmissions compared to no readmission within 180 days separately. Odds ratio (OR) and 95% confidence intervals (CIs) were reported for each risk factor of interest in the logistic regression.

In addition, due to the positive skewness of medical cost, a generalized linear model with logarithmic link function and Poisson distribution was used to assess the direct medical cost during index admission and readmission. Modified Park test was used to identify the appropriate variance function. The direct medical cost was further adjusted by known factors such as the patient's age, gender, burden of comorbidity (using ECs), severity of diabetes-related complications (using DCSI) and length of stay [26–28].

Sensitivity analysis

Since there is no consensus on the best method for measuring the burden of comorbidity for readmission studies, we sought to measure comorbidity burden using alternative measure that is commonly used for EMRs/ administrative data such as the Deyo-CCI [23], which was modified (referred to as mCCI henceforth) to exclude two conditions pertaining to diabetes from the model.

Next, as an alternative to the overall average PDC, we considered a patient to be adherent if (i) all the drug classes had a PDC of at least 0.8 or (ii) if any of the drug classes had a PDC of at least 0.8.

We also considered adopting a categorization based on a 3 rather than 6-month interval for HbA1c measurement as part of the sensitivity analysis as MOH recommends HbA1c measures at 3 to 4-month intervals for patients with "unstable glycemic control, failure to meet treatment goals, recent adjustment in therapy, or intensive insulin therapy" [29].

The Akaike information criterion (AIC) was assessed alongside the multivariable logistic regressions such that the model with the lowest AIC value indicates the preferred regression model.

RESULTS

Study population

5,124 out of 8,286 (61.8%) patients admitted during the study period fulfilled the inclusion and exclusion criteria (Figure 1); majority (66.3%) did not readmit within 180 days. 214 patients readmitted due to the same ACSC (excluding 661 patients who readmitted due to non-ACSC during their index admission). The baseline characteristics of patients who had unplanned readmissions either within 30 days or 31-180 days, or those who did not readmit within 180 days were different (Table 1).

Risk factors of unplanned readmissions

Multivariable logistic regression (Table 2) performed to identify independent risk factors associated with early unplanned readmission showed that patients that were 65 years old and above were more likely to be readmitted than those between 21 and 64 years old (OR 1.47; 95%CI 1.23-1.77). Other variables that were associated with a higher odds of early unplanned readmission included having an unplanned index admission (OR 1.69; 95%CI 1.27-2.25), longer length of index stay (OR 1.02; 95%CI 1.01-1.02), higher DCSI score (OR 1.17; 95%CI 1.09-1.26), cardiac arrhythmia (OR 1.67; 95%CI 1.25-2.23), chronic obstructive pulmonary disease (OR 1.58; 95%CI 1.11-2.23), renal failure (OR 1.84; 95%CI 1.42-2.38), liver disease (OR 1.73; 95%CI 1.06-2.82), lymphoma (OR 3.29; 95%CI 1.13-9.61), metastatic cancer (OR 2.89; 95%CI 1.54-5.43) and deficiency anemia (OR 1.31; 95%CI 1.03-1.67). Modification of diabetes-related medication was associated with a lower odds of readmission (OR 0.81; 95%CI 0.67-0.98).

For late unplanned readmission, ethnic groups other than Malay and Indian had a higher odds of readmission than Chinese (OR 1.67; 95%CI 1.24-2.24) while those aged 65 years and above had a higher odds of admission than those between 21 and 64 years old (OR 1.36; 95%CI 1.16-1.60). Patients had a higher odds of late unplanned readmission when they had an unplanned index admission (OR 2.07; 95%CI 1.59-2.70), admitted due to chronic ACSCs during their index stay relative to those who admitted due to non-ACSC (OR 1.22; 95%CI 1.01-1.48), had higher DCSI score (OR 1.18; 95%CI 1.10-1.26), congestive heart failure (OR 1.38; 95%CI 1.06-1.79), other neurological disorders (OR 2.06; 95%CI 1.44-2.96), renal failure (OR 1.45; 95%CI 1.15-1.84), lymphoma (OR 3.80; 95%CI 1.34-10.74), metastatic cancer (OR 2.29; 95%CI 1.29-4.08), and solid tumor without metastasis (OR 1.63; 95%CI 1.13-2.35). Modification to their diabetes-related medication was associated with a lower odds of readmission (OR 0.80; 95%CI 0.67-0.95). Patients who had diabetes-related medication dispensed but were not adherent were more likely to have late unplanned readmissions compared to those who did not have any diabetes-related medication dispensed during the study period (OR 1.96; 95%CI 1.40-2.76); likewise for those that had diabetes-related medication dispensed and were adherent to their diabetes-related medication (OR 1.28; 95%CI 1.08-1.52).For the sensitivity analysis, the model with the best fit based on the AIC (Table 3) was the one comprising ECs, HbA1c level obtained 3 months before index discharge and average PDC to define adherence of diabetes-related medication for both early and late unplanned readmissions. In general, variables that were associated with early or late unplanned readmissions continued to show an association with similar effect size in the multivariable analysis even after the specified variables were changed. The results from the model with the best model fit are presented in Table 4.

Cost of admissions

The mean cost of index admission for those with no readmission (US$5,520; 95%CI: US$5,518-5,523) was lower than that of early (US$6,970; 95%CI: US$6,964-6,976) or late (US$5,829; 95%CI: US$5,824-5,834) unplanned readmission while patients with early unplanned readmission (US$6,243; 95%CI: US$6,238-6,249) had a higher mean cost than those with late unplanned readmission (US$5,812; 95%CI: US$5,807-5,817) even after adjustment (Table 5). In addition, using mCCI to measure the burden of comorbidity for the cost analysis gave similar estimates as the ECs.

DISCUSSION

This study not only investigates risk factors (medication modification and adherence, severity of diabetes complications (using DCSI) and burden of comorbidities) that are not commonly investigated collectively for unplanned readmissions, but also estimates the medical costs associated with each admission (which is usually missing in such readmission studies).

Several interesting findings pertaining to the differences observed between early unplanned readmissions and late unplanned readmissions from the multivariable analysis were noted. For example, similar to the results from Graham et al [15], the length of index admission (a marker of acute illness burden) reached statistical significance for early unplanned readmission but not with late unplanned readmission in the multivariable analysis. However, as the odds ratio for length of index admission for both types of unplanned readmissions were close to 1 and have similar effect sizes, further investigation will be needed to discern the ‘true’ association between length of index admission and both types of unplanned readmissions.

Next, chronic ACSCs (being the primary reason for index admission) and diabetes-related medication adherence were associated with late unplanned readmission only. The latter is a patient-related health behavior which is potentially modifiable [30] while the former could reflect patient’s choice as patients may be choosing hospital services over primary care services for chronic disease management [31]. This raises the possibility that unlike early unplanned readmission, late unplanned readmission could be reduced by changing patient's behavior. This difference could also suggest different intervention points along the care pathway where clinical decision support/predictive models could be applied. Understanding the differences in risk factors for early or late unplanned readmission may help to better target patient referral to different types of care providers, whether short-term post-hospitalization transitional care programs or long-term care support in a home/day-care setting; it may also help to define changing priorities for supportive care as the patient progresses over time.

On the other hand, there were several risk factors associated with both early and late unplanned readmissions. Firstly, elderly patients aged 65 years and above were found to be more likely to be admitted than those aged 21-64 years old for both early unplanned readmissions and late unplanned readmissions, consistent with policies targeting elderly patients and previous findings [22].

Secondly, the ECs and mCCI were associated with early unplanned readmissions and late unplanned readmissions as both include chronic and acute disease components. Furthermore, modification of diabetes-related medication during index admission could potentially be a useful approach for reducing unplanned readmission but further investigations need to be done to determine if these modifications are genuinely advised by their physicians.

Discharge against medical advice was not associated with early or late unplanned readmissions, possibly due to the small proportion of this category of patients (1.2%) in this study. In addition, consistent with past studies, HbA1c result was not associated with either early or late unplanned readmission [32].

Results from the cost analysis show that the index admission of patients with early or late unplanned readmission cost more than that of patients with no readmissions. This finding suggests that patients who tend to be readmitted are more complex cases than patients with no readmissions as the former tend to have a higher baseline severity of diabetes complications and burden of comorbidities.

Based on the literature review, this study is the first to investigate the risk factors of both early unplanned readmissions and late unplanned readmissions among type 2 diabetes patients while taking into consideration the combination of the severity of diabetes-related complication, burden of comorbidities as well as diabetes-related medication modification and its adherence.

However, this study has a few key limitations. Firstly, although the use of EMRs minimizes recall bias as data is being recorded prospectively, due to the limited availability of background variables in the EMR, sociodemographic factors such as employment status, education level and income level which may affect the probability of readmission were not captured [33]. Likewise, non-medical issues such as inpatient diabetes education [34], physician’s prescribing behavior [35] or patient’s physical activity [36], their behavior or social network that could potentially affect the rate of readmissions as suggested by previous studies [37] could not be assessed.

Secondly, the use of a dichotomous variable compared to a continuous variable to measure medication adherence may have a lower sensitivity (proportion of adherent patients correctly identified as adherent) due to the derivation of a threshold value without a general pharmacological basis [38]. Furthermore, there is a lack of standardization across measures of medication adherence for multiple concurrent medications, which was attempted to account for by using different approaches in the sensitivity analysis. Despite using prescription-based measure of PDC instead of a 180-day interval-based measure of PDC to measure medication adherence, the majority of the study population were not found to have any diabetes-related medication dispensed before their index admission. 81% of those who did not have diabetes-related medication dispensed before index admission started diabetes-related medication after their index admission, while the remaining could have been on medications for other concurrent medical conditions (e.g. cancer or heart failure) that may cause adverse drug-drug interactions. It should be noted that even though diabetes-related medication adherence was associated with late unplanned readmission, the underlying reason may be due to the act of having diabetes-related medication dispensed, rather than adherence to diabetes-related medication itself.

Thirdly, medication dispensed as recorded in the EMR was assumed to be equivalent to medication consumed by the patients but there is no guarantee that patients will take their medications according to the frequency as prescribed. An alternative source to measure medication adherence could involve the use of electronic monitors that can provide real-time data on medication adherence based on pill bottle opening behavior [39] as well as avoid the recall bias observed when using self-reports. However, this approach could introduce a Hawthorne effect and is more expensive than the use of EMR and self-reports. Furthermore, the proportion of patients with modification to their diabetes-related medication may be overestimated. Based on information available in the EMR, patients who might not have had medication dispensed due to already having sufficient quantities of medication on hand, versus those who were genuinely advised by their physicians to stop diabetes treatment could not be differentiated. Moreover, patients could have collected their diabetes medications from other healthcare institutions as long as they had a valid prescription.

Lastly, the cost of readmission may be overestimated because it includes all health expenditure of a patient with type 2 diabetes, even if the hospital services rendered are not directly related to type 2 diabetes. On the other hand, readmission rates could be underestimated because patients could have readmitted to another healthcare facility which would not be captured in this database. Therefore, future work could include expanding the analysis to more hospitals.

CONCLUSIONS

Based on our findings, hospitals could focus on different intervention points along the care pathway and further evaluate potential strategies and interventions that target specific high-risk type 2 diabetes patient populations for early and late unplanned readmissions separately. Future work could include a prediction model for early and late unplanned readmissions based on data from multiple hospital sites and/or extended study period.

TRANSPARENCY

Declaration of funding

None.

Declaration of financial/other relationships

None.

Author contributions

MEP, JY, CC and HLW were involved in the conception and design of the study. MEP analyzed the data while MEP, JY, HLW, EST were involved in the interpretation of the data. MEP and JY were involved in the drafting of the paper. All authors agree to be accountable for all aspects of the work. All authors provided critically revised the manuscript for intellectual content, agreed to be accountable for all aspects of the work and provided the final approval of the version to be published.

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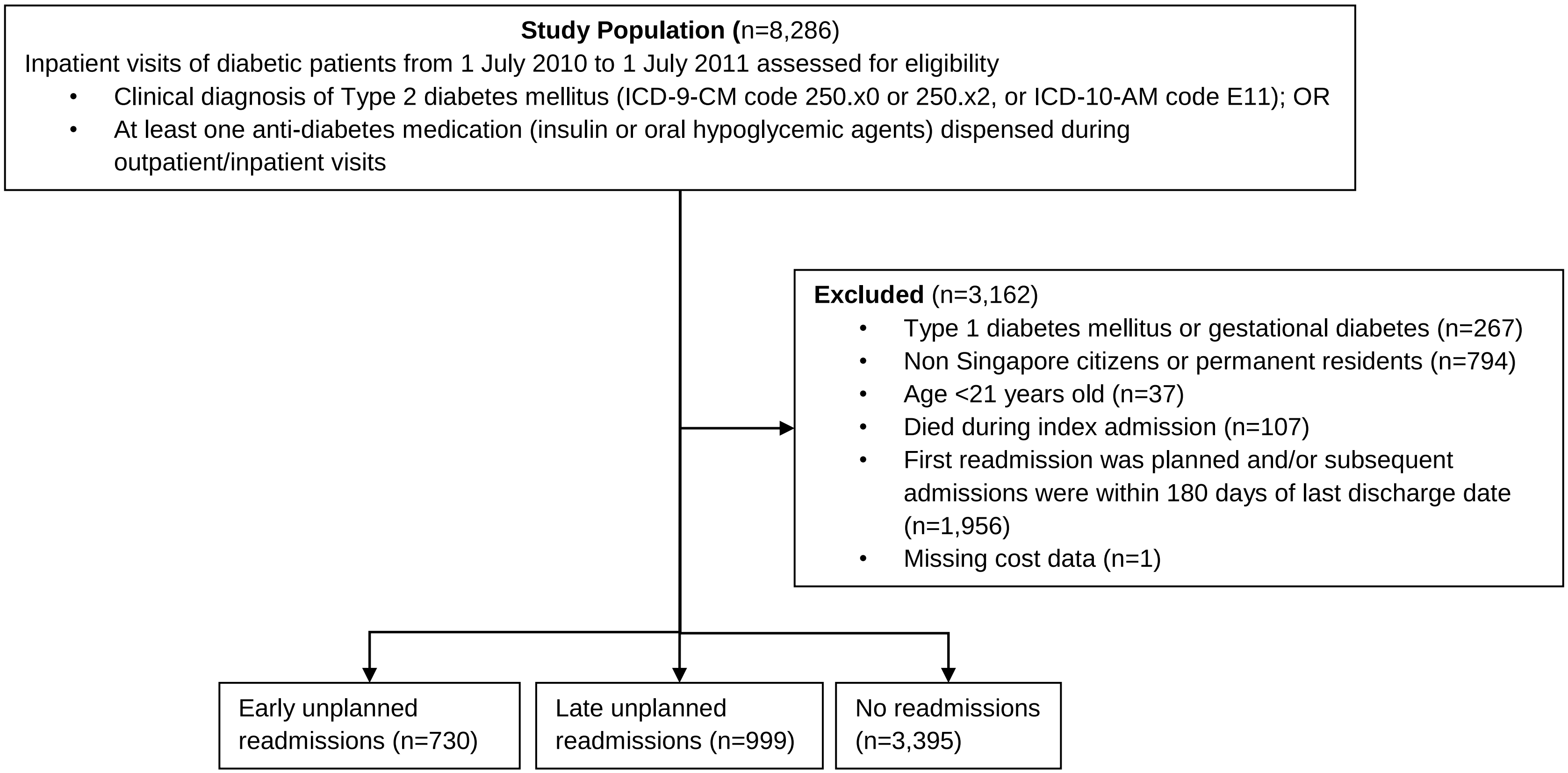
Figure 1. Flowchart of patients who met the inclusion/exclusion criteria in this study.



TABLES

Table 1. Baseline characteristics of type 2 diabetes patients with early unplanned readmission, late unplanned readmission or no readmission

Characteristics	Early unplanned readmission (n=730)	Late unplanned readmission (n=999)	No readmission (n=3,395)	p
Male (%)	378 (51.8)	487 (48.7)	1,781 (52.5)	0.119
Ethnicity (%)				<0.001
Chinese	463 (63.4)	586 (58.7)	2,041 (60.1)	
Malay	136 (18.6)	197 (19.7)	662 (19.5)	
Indian	84 (11.5)	132 (13.2)	524 (15.4)	
Others	47 (6.4)	84 (8.4)	168 (4.9)	
Age (%)				<0.001
21-64 years old	284 (38.9)	412 (41.2)	1,804 (53.1)	
65 years old and above	446 (61.1)	587 (58.8)	1,591 (46.9)	
Discharge against medical advice (%)	10 (1.4)	13 (1.3)	38 (1.1)	0.798
Unplanned index admission (%)	660 (90.4)	915 (91.6)	2,812 (82.8)	<0.001
Median length of index stay, days (25^{th}-75^{th} percentile)	4 (2-9)	4 (2-7)	3 (1-6)	<0.001
Primary reason for index admission (%)				<0.001*
Non-ACSC	445 (61.0)	574 (57.5)	2,257 (66.5)	
Chronic ACSC:	189 (25.9)	296 (29.6)	740 (21.8)	
Lower extremity amputation	17 (2.3)	9 (0.9)	39 (1.1)	
Short-term diabetes	6 (0.8)	7 (0.7)	34 (1.0)	
Long-term diabetes	66 (9.0)	105 (10.5)	261 (7.7)	
Uncontrolled diabetes	5 (0.7)	9 (0.9)	44 (1.3)	
Hypertension	5 (0.7)	13 (1.3)	31 (0.9)	
Heart failure	57 (7.8)	83 (8.3)	99 (2.9)	
Angina without procedure	22 (3.0)	40 (4.0)	146 (4.3)	
Chronic obstructive pulmonary disease	6 (0.8)	12 (1.2)	17 (0.5)	
Asthma	4 (0.5)	12 (1.2)	48 (1.4)	
Acute bronchitis	1 (0.1)	6 (0.6)	21 (0.6)	

Acute ACSC:	96 (13.2)	129 (12.9)	398 (11.7)	
Acute kidney failure	7 (1.0)	8 (0.8)	27 (0.8)	
Urinary tract infection	36 (4.9)	43 (4.3)	150 (4.4)	
Bacterial pneumonia	38 (5.2)	36 (3.6)	90 (2.7)	
Perforated appendix	1 (0.1)	0 (0.0)	3 (0.1)	
Gastroenteritis	11 (1.5)	28 (2.8)	100 (2.9)	
Dehydration	3 (0.4)	13 (1.3)	28 (0.8)	
Hyperosmolality and/or hypernatremia	0 (0.0)	1 (0.1)	0 (0.0)	
Primary reason for readmission (%)				0.499*
Non-ACSC	387 (53.0)	548 (54.9)		
Chronic ACSC:	206 (28.2)	285 (28.5)		
Lower extremity amputation	19 (2.6)	18 (1.8)		
Short-term diabetes	5 (0.7)	7 (0.7)		
Long-term diabetes	83 (11.4)	91 (9.1)		
Uncontrolled diabetes	1 (0.1)	6 (0.6)		
Hypertension	8 (1.1)	14 (1.4)		
Heart failure	54 (7.4)	86 (8.6)		
Angina without procedure	23 (3.2)	36 (3.6)		
Chronic obstructive pulmonary disease	2 (0.3)	14 (1.4)		
Asthma	6 (0.8)	12 (1.2)		
Acute bronchitis	5 (0.7)	1 (0.1)		
Acute ACSC:	137 (18.8)	166 (16.6)		
Acute kidney failure	17 (2.3)	15 (1.5)		
Urinary tract infection	52 (7.1)	64 (6.4)		
Bacterial pneumonia	45 (6.2)	46 (4.6)		
Perforated appendix	0 (0.0)	0 (0.0)		
Gastroenteritis	18 (2.5)	31 (3.1)		
Dehydration	5 (0.7)	10 (1.0)		
Hyperosmolality and/or hypernatremia	0 (0.0)	0 (0.0)		
Median DCSI (25^{th}-75^{th} percentile)	2 (0-2)	2 (0-2)	0 (0-2)	<0.001
ECs (%)				
Congestive heart failure	103 (14.1)	159 (15.9)	240 (7.1)	<0.001

Cardiac arrhythmia	92 (12.6)	98 (9.8)	215 (6.3)	<0.001
Valvular disease	54 (7.4)	63 (6.3)	147 (4.3)	0.001
Pulmonary circulation disorders	8 (1.1)	17 (1.7)	31 (0.9)	0.109
Peripheral vascular disease	59 (8.1)	56 (5.6)	141 (4.2)	<0.001
Hypertension	580 (79.5)	805 (80.6)	2,478 (73.0)	<0.001
Paralysis	28 (3.8)	57 (5.7)	124 (3.7)	0.015
Other neurological disorders	32 (4.4)	57 (5.7)	90 (2.7)	<0.001
Chronic obstructive pulmonary disease	53 (7.3)	71 (7.1)	169 (5.0)	0.006
Hypothyroidism	12 (1.6)	17 (1.7)	36 (1.1)	0.174
Renal failure	161 (22.1)	192 (19.2)	322 (9.5)	<0.001
Liver disease	27 (3.7)	23 (2.3)	76 (2.2)	0.065
Peptic ulcer disease excluding bleeding	20 (2.7)	36 (3.6)	75 (2.2)	0.046
AIDS/ HIV	3 (0.4)	1 (0.1)	2 (0.1)	0.041
Lymphoma	7 (1.0)	8 (0.8)	8 (0.2)	0.005
Metastatic cancer	27 (3.7)	35 (3.5)	44 (1.3)	<0.001
Solid tumor without metastasis	56 (7.7)	82 (8.2)	162 (4.8)	<0.001
RA/ collagen vascular diseases	0 (0.0)	6 (0.6)	22 (0.6)	0.095
Coagulopathy	40 (5.5)	55 (5.5)	134 (3.9)	0.04
Obesity	3 (0.4)	7 (0.7)	21 (0.6)	0.734
Weight loss	3 (0.4)	3 (0.3)	9 (0.3)	0.802
Fluid and electrolyte disorders	187 (25.6)	265 (26.5)	629 (18.5)	<0.001
Blood loss anemia	29 (4.0)	31 (3.1)	102 (3.0)	0.396
Deficiency anemia	157 (21.5)	200 (20.0)	427 (12.6)	<0.001
Alcohol abuse	2 (0.3)	6 (0.6)	21 (0.6)	0.524
Drug abuse	0 (0.0)	0 (0.0)	4 (0.1)	0.361
Psychoses	10 (1.4)	14 (1.4)	42 (1.2)	0.901
Depression	11 (1.5)	27 (2.7)	47 (1.4)	0.015
Median modified CCI (25th-75th percentile)	1 (0-2)	1 (0-2)	0 (0-1)	<0.001
Modification of diabetes-related drug (%)	527 (72.2)	732 (73.3)	2,592 (76.3)	0.019
Diabetes-related drug adherence before index admission, using mean PDC (%)				<0.001
Not dispensed	442 (60.5)	549 (55.0)	2,269 (66.8)	
Dispensed and not adherent	41 (5.6)	67 (6.7)	114 (3.4)	

Dispensed and adherent	247 (33.8)	383 (38.3)	1,012 (29.8)	
Diabetes-related drug adherence before index admission, using all PDC≥0.8 (%)				<0.001
Not dispensed	442 (60.5)	549 (55.0)	2,269 (66.8)	
Dispensed and not adherent	88 (12.1)	140 (14.0)	265 (7.8)	
Dispensed and adherent	200 (27.4)	310 (31.0)	861 (25.4)	
Diabetes-related drug adherence before index admission, using at least one PDC≥0.8 (%)				<0.001
Not dispensed	442 (60.5)	549 (55.0)	2,269 (66.8)	
Dispensed and not adherent	15 (2.1)	21 (2.1)	38 (1.1)	
Dispensed and adherent	273 (37.4)	429 (42.9)	1,088 (32.0)	
HbA1c level, 6 months before index discharge (%)				0.013
No HbA1c measurement	252 (34.5)	338 (33.8)	1,268 (37.3)	
Measured and not optimal	291 (39.9)	425 (42.5)	1,427 (42.0)	
Measured and optimal	187 (25.6)	236 (23.6)	700 (20.6)	
HbA1c level, 3 months before index discharge (%)				0.024
No HbA1c measurement	282 (38.6)	384 (38.4)	1,387 (40.9)	
Measured and not optimal	277 (37.9)	402 (40.2)	1,378 (40.6)	
Measured and optimal	171 (23.4)	213 (21.3)	630 (18.6)	

*Pearson's chi-square test was performed among chronic ACSC, acute ACSC and non-ACSC

Abbreviation: ACSC=Ambulatory care sensitive condition; CCI=Charlson comorbidity index; DCSI=Diabetes complication severity index; ECs=Elixhauser comorbidities; HbA1c=Glycated hemoglobin; PDC=Proportion of days covered; RA=Rheumatoid arthritis

Table 2. Multivariable logistic regression of type 2 diabetes patients with early or late unplanned readmissions

Variables	Early unplanned readmission			Late unplanned readmission		
	OR	p	95%CI	OR	p	95%CI
Gender						
Male	1.00			1.00		
Female	0.97	0.775	0.82,1.16	1.09	0.276	0.93,1.27
Ethnicity						
Chinese	1.00			1.00		
Malay	0.95	0.624	0.75,1.18	1.06	0.589	0.87,1.29
Indian	0.85	0.236	0.65,1.11	1.02	0.836	0.82,1.29
Others	1.24	0.241	0.87,1.77	1.67	0.001	1.24,2.24
Age						
21-64 years old	1.00			1.00		
65 years old and above	1.47	<0.001	1.23,1.77	1.36	<0.001	1.16,1.60
Discharge against medical advice	1.22	0.603	0.58,2.53	0.98	0.945	0.50,1.90
Unplanned index admission	1.69	<0.001	1.27,2.25	2.07	<0.001	1.59,2.70
Length of index stay	1.02	<0.001	1.01,1.02	1.00	0.586	0.99,1.01
Primary reason for index admission						
Non-ACSC	1.00			1.00		
Acute ACSC	0.98	0.879	0.75,1.28	1.04	0.749	0.82,1.32
Chronic ACSC	0.97	0.801	0.78,1.21	1.22	0.040	1.01,1.48
DCSI	1.17	<0.001	1.09,1.26	1.18	<0.001	1.10,1.26
ECs						
Congestive heart failure	1.15	0.381	0.84,1.55	1.38	0.017	1.06,1.79
Cardiac arrhythmia	1.67	<0.001	1.25,2.23	1.17	0.278	0.88,1.54
Valvular disease	1.30	0.168	0.90,1.88	1.05	0.800	0.74,1.48
Pulmonary circulation disorders	0.44	0.057	0.19,1.03	0.94	0.845	0.48,1.82
Peripheral vascular disease	1.09	0.661	0.75,1.57	0.74	0.106	0.52,1.07
Hypertension	1.08	0.497	0.87,1.33	1.13	0.218	0.93,1.36
Paralysis	0.76	0.243	0.48,1.20	1.36	0.092	0.95,1.94
Other neurological disorders	1.49	0.076	0.96,2.31	2.06	<0.001	1.44,2.96
Chronic obstructive pulmonary disease	1.58	0.010	1.11,2.23	1.32	0.079	0.97,1.81
Hypothyroidism	1.16	0.685	0.56,2.39	1.15	0.664	0.61,2.15
Renal failure	1.84	<0.001	1.42,2.38	1.45	0.002	1.15,1.84
Liver disease	1.73	0.027	1.06,2.82	1.00	0.995	0.60,1.67
Peptic ulcer disease excluding bleeding	0.96	0.881	0.55,1.66	1.42	0.127	0.91,2.21
Lymphoma	3.29	0.029	1.13,9.61	3.80	0.012	1.34,10.74
Metastatic cancer	2.89	0.001	1.54,5.43	2.29	0.005	1.29,4.08
Solid tumor without metastasis	1.31	0.214	0.86,1.99	1.63	0.009	1.13,2.35
RA/ collagen vascular diseases				0.89	0.811	0.35,2.30
Coagulopathy	0.83	0.361	0.55,1.24	1.03	0.889	0.72,1.46
Obesity	0.83	0.770	0.24,2.90	1.09	0.847	0.44,2.75
Weight loss	1.05	0.948	0.26,4.26	0.92	0.901	0.24,3.56

Fluid and electrolyte disorders	1.03	0.802	0.83,1.28	1.05	0.620	0.87,1.27
Blood loss anemia	0.70	0.148	0.44,1.13	0.65	0.053	0.41,1.01
Deficiency anemia	1.31	0.026	1.03,1.67	1.22	0.070	0.98,1.51
Alcohol abuse	0.53	0.408	0.12,2.39	1.29	0.608	0.49,3.36
Psychoses	1.28	0.517	0.61,2.68	1.04	0.900	0.54,2.01
Depression	0.86	0.683	0.43,1.74	1.58	0.082	0.94,2.65
Modification of diabetes-related drug	0.81	0.033	0.67,0.98	0.80	0.012	0.67,0.95
Diabetes-related drug adherence before index admission, using average PDC						
Not dispensed	1.00			1.00		
Dispensed and not adherent	1.48	0.056	0.99,2.22	1.96	<0.001	1.40,2.76
Dispensed and adherent	0.99	0.921	0.81,1.21	1.28	0.005	1.08,1.52
HbA1c level, 6 months before index discharge						
No HbA1c measurement	1.00			1.00		
Measured and not optimal	0.94	0.556	0.77,1.15	0.95	0.611	0.80,1.14
Measured and optimal	1.03	0.799	0.82,1.30	0.94	0.573	0.77,1.16

Note: There were no patients with rheumatoid arthritis/ collagen vascular diseases for early unplanned readmission.

Abbreviation: ACSC=Ambulatory care sensitive condition; CI=Confidence interval; DCSI=Diabetes complication severity index; ECs=Elixhauser comorbidities; HbA1c=Glycated hemoglobin; OR=Odds ratio; PDC=Proportion of days covered; RA=Rheumatoid arthritis

Table 3. Akaike information criterion of the regression models used in sensitivity analysis

		Medication adherence		
		Average PDC	All PDC≥0.8	At least one PDC≥0.8
Early unplanned readmission				
ECs	HbA1c (6 months)	3629.99	3631.36	3631.85
	HbA1c (3 months)	3629.66	3631.07	3631.51
mCCI	HbA1c (6 months)	3636.58	3637.23	3638.75
	HbA1c (3 months)	3636.25	3636.99	3638.39
Late unplanned readmission				
ECs	HbA1c (6 months)	4442.14	4444.31	4446.63
	HbA1c (3 months)	4441.94	4444.11	4446.37
mCCI	HbA1c (6 months)	4444.51	4445.23	4449.11
	HbA1c (3 months)	4444.07	4444.85	4448.6

Abbreviation: AIC=Akaike information criterion; ECs=Elixhauser comorbidities; HbA1c=Glycated hemoglobin; mCCI=Modified Charlson comorbidity index; PDC=Proportion of days covered

Table 4. Multivariable logistic regression of model with the best fit

	Early unplanned readmission			Late unplanned readmission		
	OR	p	95%CI	OR	p	95%CI
Gender						
Male	1.00			1.00		
Female	0.98	0.778	0.82,1.16	1.09	0.280	0.93,1.27
Ethnicity						
Chinese	1.00			1.00		
Malay	0.95	0.628	0.75,1.18	1.06	0.576	0.87,1.29
Indian	0.85	0.237	0.65,1.11	1.03	0.820	0.82,1.29
Others	1.24	0.236	0.87,1.78	1.67	0.001	1.24,2.25
Age						
21-64 years old	1.00			1.00		
65 years old and above	1.47	<0.001	1.23,1.76	1.36	<0.001	1.16,1.59
Discharge against medical advice	1.22	0.600	0.58,2.54	0.98	0.954	0.50,1.91
Unplanned index admission	1.69	<0.001	1.27,2.25	2.08	<0.001	1.60,2.71
Length of index stay	1.02	<0.001	1.01,1.02	1.00	0.594	0.99,1.01
Primary reason for index admission						
Non-ACSC	1.00			1.00		
Acute ACSC	0.98	0.890	0.75,1.29	1.04	0.738	0.82,1.33
Chronic ACSC	0.97	0.793	0.78,1.21	1.22	0.038	1.01,1.48
DCSI	1.17	<0.001	1.09,1.26	1.18	<0.001	1.10,1.26
ECs						
Congestive heart failure	1.15	0.384	0.84,1.55	1.38	0.017	1.06,1.79
Cardiac arrhythmia	1.67	<0.001	1.25,2.23	1.17	0.277	0.88,1.54
Valvular disease	1.30	0.167	0.90,1.88	1.05	0.794	0.74,1.48
Pulmonary circulation disorders	0.44	0.057	0.18,1.02	0.93	0.839	0.48,1.82
Peripheral vascular disease	1.09	0.647	0.75,1.58	0.74	0.105	0.52,1.07
Hypertension	1.08	0.503	0.87,1.33	1.12	0.222	0.93,1.36
Paralysis	0.76	0.244	0.48,1.20	1.36	0.089	0.95,1.95
Other neurological disorders	1.48	0.079	0.96,2.31	2.06	<0.001	1.44,2.96
Chronic obstructive pulmonary disease	1.58	0.010	1.12,2.23	1.32	0.081	0.97,1.80
Hypothyroidism	1.16	0.683	0.57,2.39	1.15	0.668	0.61,2.14
Renal failure	1.84	<0.001	1.42,2.38	1.45	0.002	1.14,1.83
Liver disease	1.73	0.027	1.07,2.82	1.01	0.983	0.60,1.67
Peptic ulcer disease excluding bleeding	0.96	0.879	0.55,1.66	1.41	0.129	0.90,2.21
Lymphoma	3.28	0.030	1.13,9.58	3.82	0.012	1.35,10.80
Metastatic cancer	2.89	0.001	1.54,5.42	2.30	0.005	1.29,4.09
Solid tumor without metastasis	1.31	0.211	0.86,1.99	1.63	0.009	1.13,2.35
RA/ collagen vascular diseases				0.89	0.816	0.35,2.30
Coagulopathy	0.83	0.359	0.55,1.24	1.02	0.893	0.72,1.46
Obesity	0.83	0.768	0.24,2.89	1.09	0.855	0.43,2.73
Weight loss	1.05	0.946	0.26,4.26	0.92	0.899	0.24,3.55
Fluid and electrolyte disorders	1.03	0.801	0.83,1.28	1.05	0.618	0.87,1.27

Blood loss anemia	0.70	0.146	0.44,1.13	0.65	0.053	0.41,1.01
Deficiency anemia	1.31	0.027	1.03,1.67	1.22	0.073	0.98,1.51
Alcohol abuse	0.53	0.407	0.12,2.39	1.29	0.608	0.49,3.36
Psychoses	1.28	0.511	0.61,2.69	1.04	0.901	0.54,2.01
Depression	0.86	0.678	0.43,1.73	1.58	0.081	0.94,2.65
Modification of diabetes-related drug	0.81	0.032	0.67,0.98	0.80	0.013	0.68,0.96
Diabetes-related drug adherence before index admission, using average PDC						
Not dispensed	1.00			1.00		
Dispensed and not adherent	1.48	0.058	0.99,2.21	1.95	<0.001	1.39,2.74
Dispensed and adherent	0.99	0.889	0.81,1.20	1.28	0.005	1.08,1.51
HbA1c level, 3 months before index discharge						
No HbA1c measurement	1.00			1.00		
Measured and not optimal	0.94	0.575	0.77,1.15	0.94	0.459	0.79,1.11
Measured and optimal	1.07	0.591	0.85,1.34	0.95	0.602	0.77,1.16

Note: There were no patients with rheumatoid arthritis/ collagen vascular diseases for early unplanned readmission.

Abbreviation: ACSC=Ambulatory care sensitive condition; CI=Confidence interval; DCSI=Diabetes complication severity index; ECs=Elixhauser comorbidities; HbA1c=Glycated hemoglobin; OR=Odds ratio; PDC=Proportion of days covered; RA=Rheumatoid arthritis

Table 5. Unadjusted and adjusted mean cost of admission (in US$)

	Unadjusted		Adjusted (ECs)			Adjusted (mCCI)		
	Cost	95%CI	Cost	95%CI	p-value	Cost	95%CI	p-value
Index admission								
No readmission	5,323	5,321-5,326	5,520	5,518-5,523	<0.001	5,470	5,468-5,473	<0.001
Early unplanned readmission	8,245	8,238-8,251	6,970	6,964-6,976	<0.001	7,317	7,311-7,323	<0.001
Late unplanned readmission	5,757	5,752-5,762	5,829	5,824-5,834	<0.001	5,765	5,760-5,769	<0.001
Readmission								
Early unplanned readmission	6,826	6,820-6,832	6,243	6,238-6,249	<0.001	6,175	6,169-6,180	<0.001
Late unplanned readmission	5,416	5,411-5,420	5,812	5,807-5,817	<0.001	5,868	5,863-5,873	<0.001

Note: Cost were adjusted by age, gender, burden of comorbidity (ECs or mCCI), diabetes complications severity index and length of stay.

Abbreviation: CI=Confidence interval; ECs=Elixhauser comorbidities; mCCI=Modified Charlson comorbidity index

Risk Factors and Direct Medical Cost of Early versus Late Unplanned Readmissions among Diabetes Patients at a Tertiary Hospital in Singapore

SUPPLEMENTAL MATERIALS

Appendix 1

Methods – Identification of independent variables

Table of significant risk factors/predictors identified from literature review

Reference	Readmission (Days)	Population	Significant Risk factors/ Predictors	Effect size (95%CI)
Caughey et al, 2017 [1]	30	Older patients with diabetes identified from the health claims database of the Department of Veterans' Affairs	Comorbid condition: heart failure No. of prescribers ≥2 hospitalizations during 6 months before index admission	aOR = 1.49 (1.03-2.17) aOR = 1.06 (1.01-1.08) aOR = 1.79 (1.15-2.78)
Collins et al, 2017 [2]	30	Medicare patients with type 2 diabetes	Age (<65 years): 75-79 80-84 85-89 Male No. of emergency room visits Inpatient length of stay, days Baseline comorbidities: Diseases of the urinary system Fluid and electrolyte disorders Diseases of white blood cells Other nervous system disorders Diseases of the heart Respiratory failure Other lower respiratory diseases Gastrointestinal hemorrhage Liver diseases Hemodialysis	 OR = 1.25 (1.12-1.39) OR = 1.31 (1.17-1.46) OR = 1.24 (1.09-1.42) OR = 1.17 (1.09-1.25) OR = 1.20 (1.19-1.22) OR = 1.02 (1.01-1.02) OR = 1.58 (1.44-1.72) OR = 1.76 (1.64-1.89) OR = 1.43 (1.31-1.56) OR = 1.42 (1.32-1.52) OR = 1.58 (1.40-1.78) OR = 1.43 (1.32-1.54) OR = 1.57 (1.45-1.70) OR = 1.56 (1.42-1.71) OR = 1.41 (1.30-1.53) OR = 1.47 (1.28-1.70)

McCoy et al, 2017 [3]	30	Adult patients with diabetes admitted to non-federal acute care hospitals	**Readmission for severe dysglycemia** Age (vs. <45 years): 45-64 65-74 ≥75 Race (vs. White): Black Other/unknown Annual income (vs. <US$40,000): 40-49,000 75-99,000 ≥100,000 Reason for index hospitalization (vs. Other causes): Hypoglycemia Hyperglycemia Unspecified Planned index hospitalization Length of stay (vs. 2-4 days): 1 5-7 8-14 ≥15 Prior hospitalizations (vs. None): Other causes Severe dysglycemia Diabetes Complications Severity Index (vs. 0): 1-2 3-6 7-29 Diabetes treatment using insulin **Readmission for other causes** Race (vs. White): Black Hispanic Annual income (vs. <US$40,000):	**Readmission for severe dysglycemia** RRR = 0.52 (0.43, 0.64) RRR = 0.56 (0.46, 0.69) RRR = 0.60 (0.49, 0.74) RRR = 1.22 (1.07, 1.38) RRR = 0.69 (0.50, 0.97) RRR = 0.77 (0.64, 0.93) RRR = 0.79 (0.66, 0.95) RRR = 0.77 (0.65, 0.91) RRR = 4.74 (3.81, 5.89) RRR = 8.57 (7.08, 10.37) RRR = 5.81 (2.00, 16.83) RRR = 0.57 (0.47, 0.69) RRR = 0.79 (0.67, 0.93) RRR = 1.42 (1.25, 1.62) RRR = 1.85 (1.60, 2.15) RRR = 2.42 (1.91, 3.07) RRR = 1.27 (1.13, 1.42) RRR = 5.47 (4.60, 6.51) RRR = 1.52 (1.25, 1.85) RRR = 2.33 (1.94, 2.81) RRR = 3.20 (2.60, 3.94) RRR = 1.79 (1.61, 1.99) **Readmission for other causes** RRR = 1.09 (1.06, 1.12) RRR = 1.05 (1.01, 1.09)

			40-49,000	RRR = 0.94 (0.91, 0.97)
			60-74,000	RRR = 0.95 (0.92, 0.98)
			75-99,000	RRR = 0.94 (0.91, 0.97)
			≥100,000	RRR = 0.90 (0.87, 0.93)
			Reason for index hospitalization (vs. Other causes):	
			Hypoglycemia	RRR = 0.87 (0.81, 0.94)
			Hyperglycemia	RRR = 0.60 (0.55, 0.67)
			Planned index hospitalization	RRR = 0.79 (0.76, 0.81)
			Length of stay (vs. 2-4 days):	
			1	RRR = 0.77 (0.75, 0.79)
			5-7	RRR = 1.35 (1.32, 1.38)
			8-14	RRR = 1.79 (1.74, 1.83)
			≥15	RRR = 2.45 (2.35, 2.55)
			Prior hospitalizations (vs. None):	
			Other causes	RRR = 1.58 (1.55, 1.61)
			Severe dysglycemia	RRR = 1.43 (1.33, 1.55)
			Diabetes Complications Severity Index (vs. 0):	
			1-2	RRR = 1.19 (1.15, 1.22)
			3-6	RRR = 1.41 (1.37, 1.45)
			7-29	RRR = 1.77 (1.72, 1.83)
			Diabetes treatment using insulin	RRR = 1.06 (1.04, 1.08)
Rubin et al, 2017 [4]	30	Adult patients with diabetes hospitalized for CVD	Home zip code <5 miles from hospital	OR = 1.52 (1.25–1.85)
			Employment status (vs. Employed):	
			Retired	OR = 1.45 (1.08–1.94)
			Disabled	OR = 1.61 (1.16–2.24)
			Education level (vs. College graduate):	
			Any high school	OR = 1.43 (1.14–1.81)
			Some college	OR = 1.38 (1.01–1.88)
			Pre-admission metformin	OR = 0.79 (0.64–0.97)
			Pre-admission sulfonylurea	OR = 1.28 (1.04–1.59)
			No. of macrovascular complications (vs. 0):	
			2	OR = 1.27 (1.07–1.51)
			3	OR = 1.42 (1.11–1.81)
			Log (admission serum creatinine)	OR = 1.23 (1.07–1.41)
			Serum albumin (vs. ≥4 g/dL):	
			Low, <4 g/dL	OR = 1.23 (1.03–1.46)
			Schizophrenia or mood disorder, current or prior	OR = 1.31 (1.07–1.60)
			Discharged within 90 days before admission	OR = 2.00 (1.69–2.36)

Rubin et al, 2016 [5]	30	Adult patients with diabetes hospitalized at an urban academic medical center	Home zip code <5 miles from hospital	OR = 1.22 (1.11-1.33)
			Employment status (vs. employed):	
			Disabled	OR = 1.94 (1.63-2.32)
			Retired	OR = 1.44 (1.22-1.69)
			Unemployed	OR = 1.52 (1.28-1.80)
			Preadmission insulin use	OR = 1.25 (1.14-1.36)
			No. of macrovascular complications (vs. 0):	
			2	OR = 1.15 (1.02-1.29)
			3	OR = 1.37 (1.17-1.61)
			4	OR = 1.43 (1.04-1.96)
			Admission serum hematocrit, per 5%	OR = 0.85 (0.82-0.88)
			Log (admission serum creatinine)	OR = 1.14 (1.07-1.22)
			Admission serum sodium (vs. normal):	
			Low, <135 mmol/L	OR = 1.32 (1.18-1.47)
			Discharged within 90 days before admission	OR = 1.93 (1.76-2.11)
			Most recent discharge status up to 1 year before admission (vs. home):	
			Against medical advice	OR = 1.49 (1.05-2.10)
			No discharge recorded	OR = 0.77 (0.70-0.85)
			Anemia, current or prior diagnosis	OR = 1.26 (1.15-1.39)
Chen et al, 2015 [6]	30	Diabetic Medicare beneficiaries who received home healthcare within 14 days of hospital discharges	Aged 75 to 84 years	HR = 1.10 (1.04-1.16)
			African American	HR = 1.11 (1.04-1.18)
			Need factors (health conditions and functional status):	
			Congestive heart failure	HR = 1.09 (1.01-1.18)
			Valvular disease	HR = 0.74 (0.59-0.92)
			Hypertension	HR = 0.82 (0.78-0.86)
			Periperal vascular disease	HR = 1.12 (1.03-1.22)
			Chronic obstructive pulmonary disease	HR = 1.60 (1.51-1.70)
			Renal failure	HR = 1.44 (1.36-1.53)
			Deficiency anemia	HR = 1.11 (1.04-1.19)
			Obesity	HR = 0.75 (0.66-0.84)
			Fluid and electrolyte diseases	HR = 1.10 (1.04-1.17)
			Psychoses	HR = 0.74 (0.59-0.93)
			Depression or anxiety	HR = 1.09 (1.04-1.14)
			Pressure or stasis ulcer	HR = 1.25 (1.16-1.35)
			Required assistance in medication management	HR = 1.16 (1.09-1.23)
			Intensity of home healthcare visits (log-transformed)	HR = 1.84 (1.77-1.91)

			Hospitals received penalty due to excess 30-day readmissions	HR = 1.21 (1.14-1.28)
Eby et al, 2015 [7]	30	Patients with type 2 diabetes identified from Humedica's de-identified electronic health records database	Surgery during index hospitalization HbA1c tested during hospitalization End-stage renal disease Heart failure Discharge disposition Any encounter within 30 days post-discharge (excluding readmission) Charlson Comorbidity Index Diabetes diagnosis prior to index stay Hypertension Payer type (vs. Uninsured): Dual eligible (Medicare/Medicaid) Medicaid Medicare Length of index stay No. of emergency room visits in the pre-period No. of inpatient visits in the pre-period Diabetic treatment escalation (vs. none–to-none): Insulin-to-insulin None-to-insulin None-to-oral Oral-to-insulin Oral-to-oral	OR = 0.88 (0.76-0.94) OR = 0.85 (0.76-0.93) OR = 1.38 (1.16-1.70) OR = 1.33 (1.15-1.60) OR = 0.84 (0.75-0.92) OR = 0.31 (0.29-0.35) OR = 1.14 (1.10-1.20) OR = 0.68 (0.61-0.76) OR = 0.80 (0.70-0.88) OR = 1.97 (1.31-2.89) OR = 1.69 (1.14-2.37) OR = 1.72 (1.17-2.43) OR = 1.11 (1.09-1.13) OR = 1.10 (1.06-1.14) OR = 1.22 (1.10-1.38) OR = 1.59 (1.32-1.94) OR = 6.56 (5.15-8.17) OR = 3.33 (2.54-4.32) OR = 3.56 (2.47-4.96) OR = 1.20 (1.03-1.37)
Raval et al, 2015 [8]	30	Elderly Medicare beneficiaries with type 2 diabetes mellitus (T2DM) aged ≥ 65 years	Cognitive impairment Falls and falls risk Polypharmacy (>13 drugs) Urinary incontinence (Adjusted for demographic, insurance, index hospitalization, clinical and healthcare utilization characteristics)	aOR = 1.06 (1.01–1.12) aOR = 1.15 (1.08–1.22) aOR = 1.20 (1.14–1.27) aOR = 1.08 (1.01–1.15)
Zapatero et al, 2014 [9]	30	Diabetes patients identified from Basic Minimum Data Set registry of the Spanish National Health System	Hypoglycemia (Adjusted for age (10 year increment), gender, Charlson comorbidity index)	aOR = 1.20 (1.17-1.23)

Healy et al, 2013 [10]	30 and 180	Patients who were hospitalized with a discharge diagnosis of diabetes and HbA1c >9%	**30 days** Diabetes education Insurance (vs. self-pay): Medicaid Log(LOS) **180 days** Diabetes education Insurance (vs. self-pay): Medicaid Medicare Log(LOS) Log(HbA1c) African American	 OR = 0.66 (0.51–0.85) OR = 1.53 (1.01–2.35) OR = 1.41 (1.21–1.64) OR = 0.80 (0.66–0.99) OR = 1.60 (1.17–2.21) OR = 1.42 (1.02–2.00) OR = 1.38 (1.22–1.57) OR = 0.46 (0.24–0.87) OR = 1.45 (1.19–1.77)
Wei et al, 2013 [11]	30	Type 2 diabetes admitted to Massachusetts General Hospital	Diabetes regimen intensification during hospitalization (Adjusted for age, index length of stay, discharge home with visiting nurse services, 'primary care physician connectedness', baseline HbA1c and Charlson comorbidity score)	aOR = 0.33 (0.12-0.88)
Albrecht et al, 2012 [12]	30	Adult patients with diabetes admitted to University of Maryland Medical Center	Serious mental illness, age <35 years Male Charlson comorbidity index >3 Length of stay >4 days	OR = 0.39 (0.17-0.91) OR = 1.21 (1.11-1.31) OR = 1.38 (1.20-1.57) OR = 1.38 (1.22-1.56)
Mokhtar et al, 2012 [13]	28	Patients with diabetes admitted to the internal medicine department	Marital status (not married) Adherence of health care providers to: Admission workup guidelines Discharge criteria guidelines	OR = 7.14 (1.13–14.1) OR = 0.91 (0.85–0.99) OR = 0.89 (0.84–0.95)
Bennett et al, 2011 [14]	30	Medicare beneficiaries with diabetes	Rurality (vs. Urban): Remote Male Age group (vs. 65-74 years): 75-84 ≥85 Race (vs. White): Other Each additional comorbidity	 OR = 0.74 (0.57-0.95) OR = 0.85 (0.78-0.92) OR = 1.11 (1.02-1.20) OR = 1.17 (1.02-1.35) OR = 0.81 (0.68-0.96) OR = 1.11 (1.02-1.20)

			Length of stay	OR = 1.11 (1.10-1.13)
			Region (vs. Northeast):	
			Midwest	OR = 0.72 (0.62-0.84)
			Had a 30-day follow-up	OR = 2.24 (1.95-2.57)
Kim et al, 2010 [15]	90	50 years or older with diabetes	Age (vs. 50 years):	
			≥80	OR = 1.07 (1.02-1.12)
			Female	OR = 0.96 (0.94-0.99)
			Race/ethnicity (vs. White):	
			Black	OR = 1.17 (1.11-1.23)
			Hispanic	OR = 1.10 (1.07-1.14)
			Primary payer (vs. Private):	
			Medicare	OR = 1.39 (1.33-1.46)
			Medicaid	OR = 1.53 (1.45-1.62)
			Resident location:	
			Urban	OR = 1.16 (1.09-1.22)
			Median income of neighborhood (vs. High):	
			Low	OR = 1.11 (1.07-1.16)
			Number of chronic conditions (vs. 1):	
			2	OR = 1.36 (1.17-1.57)
			3	OR = 1.68 (1.45-1.94)
			4	OR = 2.07 (1.79-2.39)
			5	OR = 2.36 (2.04-2.74)
			6	OR = 2.72 (2.34-3.16)
			≥7	OR = 2.93 (2.52-3.41)
			Admission history in 3 months before index hospitalization	OR = 2.17 (2.10-2.25)
			Planned admission ≥24 h in advance	OR = 1.72 (1.64-1.80)
			Disposition destination (vs. Home):	
			Other	OR = 1.28 (1.24-1.32)
			Length of stay (days)	OR = 1.02 (1.02-1.02)

Robbins et al, 2006 [16]	30	Residents with diabetes	Diabetes diagnosis (vs. Coded, had previous diagnosis): Coded, no previous diagnosis Not coded, had previous diagnosis (Adjusted for age, year, gender, race/ethnicity, insurance status, admission type, severity code, length of stay, discharge status, and number of previous hospitalizations)	 aOR = 0.46 (0.44–0.47) aOR = 1.33 (1.29–1.37)
Jiang et al, 2005 [17]	30 and 180	Diabetes patients identified from State Inpatient Databases of the Healthcare Cost and Utilization Project	**30 day** Medicare (age≥65) (vs. White): Hispanic **180 day** Private insurance (age = 18–64) (vs. White): Hispanic Medicaid (age = 18–64) (vs. White): Hispanic Medicare (age≥65) (vs. White): Black Hispanic (Adjusted for patient demographic (age, gender), socioeconomic (income at zip code, rural/urban residence), and clinical characteristics (comorbidities, complications, emergency room admission, major surgical procedure, length of stay, discharge status) during the index admission; hospital attributes (number of beds, teaching status, ownership); and dummy variables for individual states)	 aOR = 1.21 (1.12-1.30) aOR = 1.12 (1.03-1.23) aOR = 1.14 (1.05-1.24) aOR = 1.12 (1.07-1.18) aOR = 1.29 (1.23-1.36)

Abbreviation: aOR = Adjusted odds ratio; HR = Hazard ratio; OR = Odds ratio; RRR = Relative risk ratio

Appendix 2

Methods – Definition of independent variables

Primary reason for index admission

The primary reason for index admission was largely adopted from the ambulatory care sensitive conditions (ACSCs), which are conditions that can be prevented by early intervention, based on their principal diagnosis/procedure International Classification of Disease (ICD) codes captured during their index visit as defined by the U.S. Agency of Healthcare Research and Quality (AHRQ) [18]. The primary reason for index admission was categorized into acute ACSCs (acute kidney failure, urinary tract infection, bacterial pneumonia, perforated appendix, gastroenteritis, dehydration, hyperosmolality as well as hypernatremia), chronic ACSCs (lower extremity amputation, short- and long-term diabetes, uncontrolled diabetes, hypertension, heart failure, angina without procedure, chronic obstructive pulmonary disease, asthma and acute bronchitis) [19] and non-ACSCs.

Diabetes Complications Severity Index (DCSI)

The Diabetes Complications Severity Index (DCSI), identified using ICD codes and laboratory results (urine protein and serum creatinine), was utilized to measure the severity of diabetes complications [20,21]. The DCSI comprises seven categories of complications – retinopathy, nephropathy, neuropathy, cerebrovascular, cardiovascular, peripheral vascular disease and metabolic with the presence/ severity of these complications categorized into 2 or 3 levels (no abnormality = 0, some abnormality = 1 and severe abnormality = 2) [20]. We did not use a simple summation of the number of complications as prior studies have shown that DCSI performs better than the former [20].

Elixhauser comorbidities (ECs)

Comorbidity burden was measured using the Elixhauser comorbidities (ECs) [22] which categorizes the comorbidities based on ICD codes in this study because it has been demonstrated by several studies to be statistically superior to the Charlson comorbidity index (CCI) [23]. Since diabetes is the condition of interest here, two Elixhauser comorbidities related to diabetes were excluded from our analysis. Another alternative to ECs that was considered but not adopted in this study was the Elixhauser comorbidity score which is based on the summation of weights assigned to the ECs [24]. Although utilizing the ECs as a score can be better than summaries of comorbidities (e.g. comorbidity counts) and reduces overfitting risk due to the large number of comorbidities studied [24], there is a lack of meaningful clinical interpretation of the negative weights used in this score as the negative weights arise from the statistical methodology and does not denote protective effect relative to an individual without any ECs (weight=0) [25].

Diabetes-related medication

Diabetes-related medication was categorized into the following therapeutic classes in this analysis: (i) insulin; (ii) oral hypoglycemic agents (biguanide, sulphonylurea, thiazolidinedione, alpha-glucosidase inhibitors, meglitinides and dipeptidyl peptidase IV inhibitors); (iii) anti-hypertensive agents (angiotensin-converting-enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), calcium channel blockers, alpha-blockers, beta-blockers, and thiazide diuretics); and (iv) statin. Risk factors related to diabetes-related medication investigated in this include diabetes-related drug modification and adherence to diabetes-related medication.

Diabetes-related drug modification

Modification in diabetes-related medication was defined as the cessation of a therapeutic class or addition of a new therapeutic class dispensed during index discharge. A switch within the same therapeutic class (e.g. calcium channel blocker to ACE inhibitor for anti-hypertensives) was not considered to be a modification in medication. We recognize that there could be simultaneous intensification of one type of diabetes-related medication (e.g. oral hypoglycemic agent) and a de-intensification of another (e.g. statin). Hence, to simplify the analysis, we examined the overall modification instead of intensification of diabetes-related medication which previous studies have done [11,26]. As in Wei et al [11], drug dose was not captured in this analysis because the focus was on initiation or discontinuation of drugs within a therapeutic class.

Adherence to diabetes-related medication

Based on the literature review, the relationship between medication adherence and unplanned readmission among diabetes patients has never been assessed. Adherence to diabetes-related medication was assessed using prescription-based measure of proportion of days covered (PDC), which has a range of 0 to 1, measured from the first dispense date to the last dispense date of the medication such that the last dispense date occurred before the index admission date [27,28]. Switching between medications within the same drug class (e.g. glimepiride to glipizide from sulphonylurea) during the time interval was considered to be continuous intake of that drug class (sulphonylurea) and any overlap in days of supply for the drug was adjusted according to the Pharmacy Quality Alliance (PQA) specifications [27].

As patients may be taking medications from more than one therapeutic class, we calculated an average PDC based on the drug classes. For example, if a patient had two drug classes of oral hypoglycemic (biguanide and sulphonylurea) and one drug class of anti-hypertensive (beta-blocker) dispensed, the PDC for biguanide, sulphonylurea and beta-blocker would be averaged to get an overall mean PDC. A patient would be considered adherent if the overall mean PDC was at least 0.8. Medication adherence was then classified into three mutually-exclusive categories: (i) no diabetes-related medication dispensed 180 days before 1 July 2010 till before index admission, (ii) diabetes-related medication dispensed and not adherent, and (iii) diabetes-related medication dispensed and adherent.

Measurement of HbA1c level

Similar to Strack et al [29], HbA1c measurement was classified into three categories: (i) no HbA1c measurement performed within 6 months from date of index discharge, (ii) HbA1c measurement performed within 6 months from index discharge and not in the optimal range (HbA1c >7%) and (iii) HbA1c measurement performed within 6 months from index discharge and in the optimal range (HbA1c ≤7%), where the optimal level was based on the desirable target of control recommended by the local Ministry of Health (MOH) [30]. A 6-month period was used as the MOH recommends that patients with stable glycemic control who meet treatment goals have HbA1c tested within a 6-monthly interval [30].

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