**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 | aOR = 1.49 (1.03-2.17) |
| No. of prescribers | aOR = 1.06 (1.01-1.08) |
| ≥2 hospitalizations during 6 months before index admission | aOR = 1.79 (1.15-2.78) |
| Collins et al, 2017 [2] | 30 | Medicare patients with type 2 diabetes | Age (<65 years): |  |
| 75-79 | OR = 1.25 (1.12-1.39) |
| 80-84 | OR = 1.31 (1.17-1.46) |
| 85-89 | OR = 1.24 (1.09-1.42) |
| Male | OR = 1.17 (1.09-1.25) |
| No. of emergency room visits | OR = 1.20 (1.19-1.22) |
| Inpatient length of stay, days | OR = 1.02 (1.01-1.02) |
| Baseline comorbidities: |  |
| Diseases of the urinary system | OR = 1.58 (1.44-1.72) |
| Fluid and electrolyte disorders | OR = 1.76 (1.64-1.89) |
| Diseases of white blood cells | OR = 1.43 (1.31-1.56) |
| Other nervous system disorders | OR = 1.42 (1.32-1.52) |
| Diseases of the heart | OR = 1.58 (1.40-1.78) |
| Respiratory failure | OR = 1.43 (1.32-1.54) |
| Other lower respiratory diseases | OR = 1.57 (1.45-1.70) |
| Gastrointestinal hemorrhage | OR = 1.56 (1.42-1.71) |
| Liver diseases | OR = 1.41 (1.30-1.53) |
| Hemodialysis | 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** | **Readmission for severe dysglycemia** |
| Age (vs. <45 years): |  |
| 45-64 | RRR = 0.52 (0.43, 0.64) |
| 65-74 | RRR = 0.56 (0.46, 0.69) |
| ≥75 | RRR = 0.60 (0.49, 0.74) |
|  |  |  | Race (vs. White): |  |
| Black | RRR = 1.22 (1.07, 1.38) |
| Other/unknown | RRR = 0.69 (0.50, 0.97) |
| Annual income (vs. <US$40,000): |  |
| 40-49,000 | RRR = 0.77 (0.64, 0.93) |
| 75-99,000 | RRR = 0.79 (0.66, 0.95) |
| ≥100,000 | RRR = 0.77 (0.65, 0.91) |
| Reason for index hospitalization (vs. Other causes): |  |
| Hypoglycemia | RRR = 4.74 (3.81, 5.89) |
| Hyperglycemia | RRR = 8.57 (7.08, 10.37) |
| Unspecified | RRR = 5.81 (2.00, 16.83) |
| Planned index hospitalization | RRR = 0.57 (0.47, 0.69) |
| Length of stay (vs. 2-4 days): |  |
| 1 | RRR = 0.79 (0.67, 0.93) |
| 5-7 | RRR = 1.42 (1.25, 1.62) |
| 8-14 | RRR = 1.85 (1.60, 2.15) |
| ≥15 | RRR = 2.42 (1.91, 3.07) |
| Prior hospitalizations (vs. None): |  |
| Other causes | RRR = 1.27 (1.13, 1.42) |
| Severe dysglycemia | RRR = 5.47 (4.60, 6.51) |
| Diabetes Complications Severity Index (vs. 0): |  |
| 1-2 | RRR = 1.52 (1.25, 1.85) |
| 3-6 | RRR = 2.33 (1.94, 2.81) |
| 7-29 | RRR = 3.20 (2.60, 3.94) |
| Diabetes treatment using insulin | RRR = 1.79 (1.61, 1.99) |
| **Readmission for other causes** | **Readmission for other causes** |
| Race (vs. White): |  |
| Black | RRR = 1.09 (1.06, 1.12) |
| Hispanic | RRR = 1.05 (1.01, 1.09) |
| Annual income (vs. <US$40,000): |  |
| 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 | OR = 0.88 (0.76-0.94) |
| HbA1c tested during hospitalization | OR = 0.85 (0.76-0.93) |
| End-stage renal disease | OR = 1.38 (1.16-1.70) |
| Heart failure | OR = 1.33 (1.15-1.60) |
| Discharge disposition | OR = 0.84 (0.75-0.92) |
| Any encounter within 30 days post-discharge (excluding readmission) | OR = 0.31 (0.29-0.35) |
| Charlson Comorbidity Index | OR = 1.14 (1.10-1.20) |
| Diabetes diagnosis prior to index stay | OR = 0.68 (0.61-0.76) |
| Hypertension | OR = 0.80 (0.70-0.88) |
| Payer type (vs. Uninsured): |  |
| Dual eligible (Medicare/Medicaid) | OR = 1.97 (1.31-2.89) |
| Medicaid | OR = 1.69 (1.14-2.37) |
| Medicare | OR = 1.72 (1.17-2.43) |
| Length of index stay | OR = 1.11 (1.09-1.13) |
| No. of emergency room visits in the pre-period | OR = 1.10 (1.06-1.14) |
|  |  |  | No. of inpatient visits in the pre-period | OR = 1.22 (1.10-1.38) |
| Diabetic treatment escalation (vs. none–to-none): |  |
| Insulin-to-insulin | OR = 1.59 (1.32-1.94) |
| None-to-insulin | OR = 6.56 (5.15-8.17) |
|  |  |  | None-to-oral | OR = 3.33 (2.54-4.32) |
| Oral-to-insulin | OR = 3.56 (2.47-4.96) |
| Oral-to-oral | 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 | aOR = 1.06 (1.01–1.12) |
| Falls and falls risk | aOR = 1.15 (1.08–1.22) |
| Polypharmacy (>13 drugs) | aOR = 1.20 (1.14–1.27) |
| Urinary incontinence | aOR = 1.08 (1.01–1.15) |
| (Adjusted for demographic, insurance, index hospitalization, clinical and healthcare utilization characteristics) |  |
| Zapatero et al, 2014 [9] | 30 | Diabetes patients identified from Basic Minimum Data Set registry of the Spanish National Health System | Hypoglycemia | aOR = 1.20 (1.17-1.23) |
| (Adjusted for age (10 year increment), gender, Charlson comorbidity index) |  |
| 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 | OR = 0.66 (0.51–0.85) |
| Insurance (vs. self-pay): |  |
| Medicaid  | OR = 1.53 (1.01–2.35) |
| Log(LOS) | OR = 1.41 (1.21–1.64) |
|  |  |
| **180 days** |  |
| Diabetes education | OR = 0.80 (0.66–0.99) |
| Insurance (vs. self-pay): |  |
| Medicaid | OR = 1.60 (1.17–2.21) |
| Medicare | OR = 1.42 (1.02–2.00) |
| Log(LOS) | OR = 1.38 (1.22–1.57) |
| Log(HbA1c) | OR = 0.46 (0.24–0.87) |
|  |  |  | African American | 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 | aOR = 0.33 (0.12-0.88) |
| (Adjusted for age, index length of stay, discharge home  |  |
|  |  |  | with visiting nurse services, ‘primary care physician connectedness’, baseline HbA1c and Charlson comorbidity score) |  |
| Albrecht et al, 2012 [12] | 30 | Adult patients with diabetes admitted to University of Maryland Medical Center | Serious mental illness, age <35 years | OR = 0.39 (0.17-0.91) |
| Male | OR = 1.21 (1.11-1.31) |
| Charlson comorbidity index >3 | OR = 1.38 (1.20-1.57) |
| Length of stay >4 days | 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) | OR = 7.14 (1.13–14.1) |
| Adherence of health care providers to: |  |
| Admission workup guidelines | OR = 0.91 (0.85–0.99) |
| Discharge criteria guidelines | OR = 0.89 (0.84–0.95) |
| Bennett et al, 2011 [14] | 30 | Medicare beneficiaries with diabetes | Rurality (vs. Urban): |  |
| Remote | OR = 0.74 (0.57-0.95) |
| Male | OR = 0.85 (0.78-0.92) |
| Age group (vs. 65-74 years): |  |
| 75-84 | OR = 1.11 (1.02-1.20) |
| ≥85 | OR = 1.17 (1.02-1.35) |
| Race (vs. White): |  |
| Other | OR = 0.81 (0.68-0.96) |
| Each additional comorbidity | 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 | aOR = 0.46 (0.44–0.47) |
| Not coded, had previous diagnosis | aOR = 1.33 (1.29–1.37) |
| (Adjusted for age, year, gender, race/ethnicity, insurance status, admission type, severity code, length of stay, discharge status, and number of previous hospitalizations) |  |
| 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 | aOR = 1.21 (1.12-1.30) |
| **180 day** |  |
| Private insurance (age = 18–64) (vs. White): |  |
| Hispanic | aOR = 1.12 (1.03-1.23) |
| Medicaid (age = 18–64) (vs. White): |  |
| Hispanic | aOR = 1.14 (1.05-1.24) |
| Medicare (age≥65) (vs. White): |  |
| Black | aOR = 1.12 (1.07-1.18) |
| Hispanic | aOR = 1.29 (1.23-1.36) |
| (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) |  |

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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