Impact of Hypoglycemia on 30-Day Readmission and Survival Outcomes in Patients with Type 2 Diabetes Mellitus

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## Preamble:

* **Study Objective:**
* To identify patient- and hospital-level predictors of 30-day all-cause hospital readmission among adults hospitalized with T2DM using a nationally representative dataset. This study also evaluates the clinical and economic burden of readmission in this high-risk population, including its associations with in-hospital mortality, length of stay (LOS), and hospital charges.
* **Data Source:**
* A retrospective cohort study using the 2016–2017 Nationwide Readmissions Database (NRD), developed by the Healthcare Cost and Utilization Project (HCUP). The NRD enables tracking of individual patients across hospitalizations within a given year via synthetic identifiers, capturing discharges from U.S. community hospitals and supporting survey-weighted national estimates through complex sampling design.
* **Cohort Definition:**
* Index hospitalizations were included if they met all of the following criteria:
  + Adults aged ≥18 years
  + Principal diagnosis of T2DM, with or without hypoglycemia, identified using ICD-10-CM code: E1164
  + Non-elective admission
  + Index discharge by the end of November to allow for a complete 30-day follow-up period
  + Complete data on LOS and NRD\_DAYSTOEVENT, required to compute discharge dates
* **Outcomes of Interest:**
  + Primary Outcome:
    - All-cause 30-day readmission (Yes/No), flagged using NRD linkage variables
  + Secondary Outcomes (index admission):
    - In-hospital mortality (DIED)
    - Length of stay (LOS, in days)
    - Total hospitalization charges (TOTCHG), inflation-adjusted to 2017 USD
    - Non-home discharge
  + Readmission Characteristics:
    - In-hospital mortality
    - Length of stay (LOS, in days)
    - Total hospitalization charges (inflation-adjusted to 2017 USD)
* **Outcome Definitions:**
  + Readmission:
    - Defined using HCUP NRD’s methodology. Readmissions were identified only among patients with qualifying index events.
    - Trauma-related hospitalizations were excluded only from the readmission pool to avoid unrelated admissions.
  + Mortality:
    - In-hospital death recorded during index or readmission (DIED = 1)
  + LOS:
    - Reported in days; modeled as count outcome
  + Charge:
    - Derived from HCUP’s TOTCHG variable and adjusted to 2017 dollars using Consumer Price Index (CPI) data
  + Non-Home Discharge:
    - Defined as any disposition other than home/self-care, specifically:
      * Transfer to another short-term hospital
      * Transfer to skilled nursing facility (SNF), intermediate, or other facility
      * Left against medical advice
      * Died in hospital
      * Alive, destination unknown
* **Covariates and Variable Construction:**
  + Demographic & Socioeconomic Factors:
    - Age (continuous)
    - Sex (FEMALE; ref = Male)
    - Primary expected payer (Insurance; Medicare, Medicaid, Private, Other)
    - Income quartile based on ZIP code (ZIPINC\_QRTL)
    - Weekend admission (AWEEKEND)
  + Comorbidities and Clinical Covariates: (from Elixhauser and Charlson flags)
    - Congestive heart failure
    - Hypertension
    - Renal failure
    - Liver disease
    - Peripheral vascular disease
    - Chronic pulmonary disease
    - Dementia
    - Fluid and electrolyte imbalance
  + Hospital Characteristics:
    - Hospital bed size (Small, Medium, Large)
    - Urban/rural teaching status (Metropolitan, teaching vs non-teaching, etc.)
  + Disposition and Severity:
    - Non-home discharge (e.g., SNF, hospice, other facilities, or death)
    - Length of stay
* **Statistical Methods:**
  + Survey Design and Weighting:
    - All analyses accounted for NRD’s complex survey design using weights (DISCWT), strata (NRD\_STRATUM), and clustering (HOSP\_NRD). Survey-adjusted methods were implemented via survey and srvyr packages.
  + Descriptive Analyses:
    - Baseline characteristics were summarized across T2DM without hypoglcemia vs.T2DM with hypoglycemia groups using survey-weighted means/proportions.
    - P-values from design-based statistical tests (Rao–Scott adjusted chi-square for categorical variables; design-based Kruskal–Wallis test for continuous variables).
  + Multivariable Regression:
    - The model included demographic, clinical, hospital-level, and index-stay factors.
    - Hazard ratios (HRs) with 95% confidence intervals (CIs) were reported
  + Readmission Characteristics:
    - A sub-analysis among patients with 30-day readmissions summarized readmission hospitalization characteristics descriptively using weighted survey statistics.
* **Software:** All analyses were conducted in R Statistical Language (Version 4.5.0; R Foundation for Statistical Computing, Vienna, Austria).

## Descriptive Analyses

### Baseline Characteristics

| **Characteristic** | **Overall** N = 584,357*1* | **T2DM with hypoglycemia** N = 81,286*1* | **T2DM without hypoglycemia** N = 503,071*1* | **p-value***2* |
| --- | --- | --- | --- | --- |
| Age (years) |  |  |  | <0.001 |
| 18–49 | 124,338 (21%) | 5,471 (6.7%) | 118,867 (24%) |  |
| 50–64 | 226,128 (39%) | 20,571 (25%) | 205,558 (41%) |  |
| 65–79 | 168,418 (29%) | 34,323 (42%) | 134,095 (27%) |  |
| 80+ | 65,473 (11%) | 20,921 (26%) | 44,551 (8.9%) |  |
| Sex |  |  |  | <0.001 |
| Male | 340,969 (58%) | 38,769 (48%) | 302,199 (60%) |  |
| Female | 243,388 (42%) | 42,517 (52%) | 200,872 (40%) |  |
| Median Income Quartile |  |  |  | <0.001 |
| 0-25th percentile | 228,855 (40%) | 30,819 (38%) | 198,036 (40%) |  |
| 26th to 50th percentile | 154,495 (27%) | 20,854 (26%) | 133,641 (27%) |  |
| 51st to 75th percentile | 118,105 (21%) | 17,012 (21%) | 101,093 (20%) |  |
| 76th to 100th percentile | 74,439 (13%) | 11,603 (14%) | 62,836 (13%) |  |
| Hospital Bed Size |  |  |  | 0.003 |
| Small | 96,554 (17%) | 13,815 (17%) | 82,739 (16%) |  |
| Large | 318,246 (54%) | 43,126 (53%) | 275,121 (55%) |  |
| Medium | 169,556 (29%) | 24,345 (30%) | 145,212 (29%) |  |
| Hospital Teaching Status |  |  |  | <0.001 |
| Metropolitan, non-teaching | 149,745 (26%) | 22,379 (28%) | 127,366 (25%) |  |
| Metropolitan, teaching | 380,562 (65%) | 51,081 (63%) | 329,481 (65%) |  |
| Non-metropolitan | 54,049 (9.2%) | 7,826 (9.6%) | 46,224 (9.2%) |  |
| Insurance |  |  |  | <0.001 |
| Private | 101,527 (17%) | 7,354 (9.1%) | 94,173 (19%) |  |
| Medicaid | 110,215 (19%) | 8,826 (11%) | 101,389 (20%) |  |
| Other | 371,746 (64%) | 65,021 (80%) | 306,725 (61%) |  |
| Discharged to Non-Home Setting | 135,690 (23%) | 22,712 (28%) | 112,978 (22%) | <0.001 |
| No. of comorbidities |  |  |  | <0.001 |
| One comorbidity | 95,941 (16%) | 12,501 (15%) | 83,439 (17%) |  |
| Two or more comorbidities | 488,416 (84%) | 68,785 (85%) | 419,632 (83%) |  |
| Congestive heart failure | 127,508 (22%) | 24,842 (31%) | 102,666 (20%) | <0.001 |
| Liver disease | 30,014 (5.1%) | 4,455 (5.5%) | 25,559 (5.1%) | 0.002 |
| Obesity | 142,684 (24%) | 13,956 (17%) | 128,727 (26%) | <0.001 |
| Hypertension | 475,988 (81%) | 70,372 (87%) | 405,616 (81%) | <0.001 |
| Renal disease | 221,883 (38%) | 39,222 (48%) | 182,661 (36%) | <0.001 |
| Peripheral vascular disease | 92,682 (16%) | 8,783 (11%) | 83,900 (17%) | <0.001 |
| Depression | 87,222 (15%) | 12,038 (15%) | 75,184 (15%) | 0.6 |
| Chronic pulmonary disease | 107,366 (18%) | 18,927 (23%) | 88,438 (18%) | <0.001 |
| Dementia | 40,184 (6.9%) | 12,780 (16%) | 27,404 (5.4%) | <0.001 |
| Fluid and electrolyte imbalance | 248,530 (43%) | 33,493 (41%) | 215,036 (43%) | <0.001 |
| *1*n (%) | | | | |
| *2*Pearson's X^2: Rao & Scott adjustment | | | | |

### Outcomes of Index Hospitalizations

| **Characteristic** | **Overall** N = 584,357*1* | **T2DM with hypoglycemia** N = 81,286*1* | **T2DM without hypoglycemia** N = 503,071*1* | **p-value***2* |
| --- | --- | --- | --- | --- |
| 30-Day Readmission |  |  |  | <0.001 |
| Without Readmission | 501,653 (86%) | 69,271 (85%) | 432,383 (86%) |  |
| With 30-day readmission | 82,704 (14%) | 12,015 (15%) | 70,689 (14%) |  |
| In-Hospital Mortality | 4,534 (0.8%) | 1,193 (1.5%) | 3,341 (0.7%) | <0.001 |
| Length of Stay (days) | 4.0 (2.0, 7.0) | 3.0 (2.0, 4.0) | 4.0 (2.0, 7.0) | <0.001 |
| Inflation-Adjusted Total Charges ($) | 29,983 (16,168, 58,778) | 22,020 (13,207, 38,272) | 31,820 (16,877, 62,864) | <0.001 |
| Discharged to Non-Home Setting | 135,690 (23%) | 22,712 (28%) | 112,978 (22%) | <0.001 |
| *1*n (%); Median (Q1, Q3) | | | | |
| *2*Pearson's X^2: Rao & Scott adjustment; Design-based KruskalWallis test | | | | |

## Readmission Hospitalization Characteristics

### Readmission Rate:

Index hospitalizations resulted in:

1. Readmission (n): 82703
2. Readmission Rate (%): 14.15%
3. Readmission Rate (95% CI): 13.97% to 14.33%

### In-Hospital Mortality by Readmission Status:

### In-Hospital Mortality Among Readmitted Patients

Readmission hospitalizations resulted in:

1. Deaths (n): 2555
2. Death Rate (%): 3.1%
3. Death Rate (95% CI): 2.92% to 3.28%

### Resource Utilization During Readmission

Readmission hospitalizations resulted in:

1. Median Length of Stay (IQR), days: 4 (IQR: 2–7)
2. Median Total Charges (IQR): $33,580 (IQR: $18,435–$64,261)

## Multivariable Analyses

### 30-Day Readmission:

| **Characteristic** | **OR** | **95% CI** | **p-value** |
| --- | --- | --- | --- |
| Hypoglycemia categories |  |  |  |
| T2DM with hypoglycemia | — | — |  |
| T2DM without hypoglycemia | 0.94 | 0.91, 0.97 | <0.001 |
| Age (years) | 0.99 | 0.99, 0.99 | <0.001 |
| Sex |  |  |  |
| Male | — | — |  |
| Female | 1.20 | 1.17, 1.24 | <0.001 |
| Insurance |  |  |  |
| Private | — | — |  |
| Medicaid | 1.54 | 1.46, 1.61 | <0.001 |
| Other | 1.46 | 1.40, 1.51 | <0.001 |
| Median Income Quartile |  |  |  |
| 0-25th percentile | — | — |  |
| 26th to 50th percentile | 0.93 | 0.91, 0.96 | <0.001 |
| 51st to 75th percentile | 0.90 | 0.87, 0.94 | <0.001 |
| 76th to 100th percentile | 0.88 | 0.84, 0.92 | <0.001 |
| Hospital Bed Size |  |  |  |
| Small | — | — |  |
| Large | 1.02 | 0.98, 1.06 | 0.3 |
| Medium | 1.02 | 0.98, 1.07 | 0.4 |
| Hospital Teaching Status |  |  |  |
| Metropolitan, non-teaching | — | — |  |
| Metropolitan, teaching | 0.96 | 0.93, 0.99 | 0.019 |
| Non-metropolitan | 0.91 | 0.86, 0.97 | 0.002 |
| Discharged to Non-Home Setting |  |  |  |
| No | — | — |  |
| Yes | 1.11 | 1.08, 1.14 | <0.001 |
| No. of comorbidities |  |  |  |
| One comorbidity | — | — |  |
| Two or more comorbidities | 1.68 | 1.61, 1.75 | <0.001 |
| Congestive heart failure |  |  |  |
| No | — | — |  |
| Yes | 1.34 | 1.30, 1.37 | <0.001 |
| Chronic pulmonary disease |  |  |  |
| No | — | — |  |
| Yes | 1.08 | 1.05, 1.11 | <0.001 |
| Obesity |  |  |  |
| No | — | — |  |
| Yes | 0.79 | 0.76, 0.81 | <0.001 |
| Liver disease |  |  |  |
| No | — | — |  |
| Yes | 1.11 | 1.06, 1.17 | <0.001 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | 1.05 | 1.01, 1.08 | 0.008 |
| Renal disease |  |  |  |
| No | — | — |  |
| Yes | 1.28 | 1.25, 1.31 | <0.001 |
| Peripheral vascular disease |  |  |  |
| No | — | — |  |
| Yes | 1.09 | 1.05, 1.12 | <0.001 |
| Depression |  |  |  |
| No | — | — |  |
| Yes | 1.11 | 1.08, 1.15 | <0.001 |
| Dementia |  |  |  |
| No | — | — |  |
| Yes | 1.00 | 0.95, 1.05 | >0.9 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 1.11 | 1.08, 1.13 | <0.001 |
| Drug\_abuse |  |  |  |
| No | — | — |  |
| Yes | 1.39 | 1.32, 1.46 | <0.001 |
| Abbreviations: CI = Confidence Interval, OR = Odds Ratio | | | |