Original Investigation

National Trends in US Hospital Admissions for Hyperglycemia and Hypoglycemia Among Medicare Beneficiaries, 1999 to 2011

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IMPORTANCE The increasing intensity of diabetes mellitus management over the past decade may have resulted in lower rates of hyperglycemic emergencies but higher rates of hospital admissions for hypoglycemia among older adults. Trends in these hospitalizations and subsequent outcomes are not known.

OBJECTIVE To characterize changes in hyperglycemia and hypoglycemia hospitalization rates and subsequent mortality and readmission rates among older adults in the United States over a 12-year period, and to compare these results according to age, sex, and race.

DESIGN, SETTING, AND PATIENTS Retrospective observational study using data from 33,952,331 Medicare fee-for-service beneficiaries 65 years or older from 1999 to 2011.

MAIN OUTCOMES AND MEASURES Hospitalization rates for hyperglycemia and hypoglycemia, 30-day and 1-year mortality rates, and 30-day readmission rates.

RESULTS A total of 279,937 patients experienced 302,095 hospitalizations for hyperglycemia, and 404,467 patients experienced 429,850 hospitalizations for hypoglycemia between 1999 and 2011. During this time, rates of admissions for hyperglycemia declined by 38.6% (from 114 to 70 admissions per 100,000 person-years), while admissions for hypoglycemia increased by 11.7% (from 94 to 105 admissions per 100,000 person-years). In analyses designed to account for changing diabetes mellitus prevalence, admissions for hyperglycemia and hypoglycemia declined by 55.2% and 9.5%, respectively. Trends were similar across age, sex, and racial subgroups, but hypoglycemia rates were 2-fold higher for older patients (≥75 years) when compared with younger patients (65-74 years), and admission rates for both hyperglycemia and hypoglycemia were 4-fold higher for black patients compared with white patients. The 30-day and 1-year mortality and 30-day readmission rates improved during the study period and were similar after an index hospitalization for either hyperglycemia or hypoglycemia (5.4%, 17.1%, and 15.3%, respectively, after hyperglycemia hospitalizations in 2010; 4.4%, 19.9%, and 16.3% after hypoglycemia hospitalizations).

CONCLUSIONS AND RELEVANCE Hospital admission rates for hypoglycemia now exceed those for hyperglycemia among older adults. Although admissions for hypoglycemia have declined modestly since 2007, rates among black Medicare beneficiaries and those older than 75 years remain high. Hospital admissions for severe hypoglycemia seem to pose a greater health threat than those for hyperglycemia, suggesting new opportunities for improvement in care of persons with diabetes mellitus.

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Severe hypoglycemia is the most common acute adverse effect of glucose-lowering therapy among patients with diabetes mellitus (DM) and is associated with poor outcomes, including death. Several recent trials have raised questions about the benefits of intensive glucose control and have demonstrated harms associated with these strategies, including severe hypoglycemia and even mortality. Older patients, particularly those with multiple comorbidities, may derive less benefit from intensive strategies to lower glucose levels and may be more susceptible to hypoglycemia and its consequences. Despite these concerns for older patients, DM care quality metrics established more than a decade ago have primarily focused on prevention of hyperglycemia and its complications and rewarded target-based glucose lowering to achieve a hemoglobin A1c (HbA1c) level below 7% of total hemoglobin and, more recently, below 8% of total hemoglobin. These efforts have been successful, and the proportion of patients with DM achieving HbA1c levels below these thresholds improved significantly between 1999 and 2010. However, the consequences of these changes may include increased rates of hypoglycemia. (To convert HbA1c to a proportion of total hemoglobin, multiply by 0.01.)

Accordingly, we sought to characterize rates of hospital admissions for hyperglycemia and hypoglycemia during the period of time when glycemic control improved, using a 100% sample of Medicare beneficiaries from 1999 to 2011. We hypothesized that the adoption of more intensive glycemic control strategies may have reduced rates of severe hyperglycemia but may have increased hypoglycemia. Because glycemic control and complications of treatment are known to differ among elderly individuals and black adults, we also investigated whether trends in admissions for hyperglycemia and hypoglycemia differed among patients across age, sex, and racial subgroups. Given the limited data on outcomes following hospitalization for hyperglycemia and hypoglycemia, we also evaluated changes in short- and long-term mortality and readmission rates following hospitalization to understand implications of these events for older adults. Finally, using nationally representative survey data from the Centers for Disease Control and Prevention, we performed additional analyses to estimate rates of hospitalizations among Medicare beneficiaries with DM, because DM prevalence increased over the study period.

Methods

Institutional review board approval was obtained through the Yale University Human Investigation Committee, and the requirement for informed consent was waived based on the nature of the study. We used inpatient National Claims History files from the Centers for Medicare and Medicaid Services (CMS) to identify all fee-for-service (FFS) Medicare beneficiaries from 1999 to 2011 and excluded beneficiaries if they were younger than 65 years or were hospitalized or resided outside of the 50 US states, the District of Columbia, and Puerto Rico.

Main Outcome Measures

To characterize relevant DM events among Medicare beneficiaries, we examined the following 5 outcome measures: hyperglycemia and hypoglycemia hospitalization rates, subsequent 30-day and 1-year mortality, and 30-day readmission rates.

Hyperglycemia and Hypoglycemia Hospitalization Rates

We defined hospitalizations for hyperglycemia and hypoglycemia as admissions to an acute care hospital for a principal discharge diagnosis of hyperglycemia or hypoglycemia based on validated methods (eTable 1 in the Supplement). The outcomes did not include observation stays, emergency department visits, or secondary diagnoses of hyperglycemia or hypoglycemia (because they may have occurred during hospitalization or secondary to another acute event). For each year, we calculated hospitalization rates by dividing the total number of hospital admissions for hyperglycemia or hypoglycemia (numerator) by the total accumulated person-years of time (denominator). Because our intent was to describe the overall burden of these hospitalizations on the health care system, the denominator included all eligible Medicare FFS beneficiaries and was not limited to persons with DM. The use of all eligible beneficiaries also ensured that the denominator was standardized over time and was not affected by changes in the severity of diagnosed DM. To account for new enrollment, disenrollment, or death during an index year, we calculated person-years for each beneficiary. All rates are reported per 100,000 person-years.

30-Day and 1-Year Mortality Outcomes

For all patients admitted for hyperglycemia and hypoglycemia in a given year, we determined 30-day and 1-year mortality using the CMS vital status file (which included in-hospital and out-of-hospital mortality). If a patient had more than 1 admission in a given year, 1 hospitalization was selected at random. The admission date represented “time zero” for the mortality analysis. We then examined the proportion of patients who died within the 30-day and 1-year of admission.

30-Day Readmission Outcome

To generate 30-day all-cause readmission rates, we calculated the proportion of patients who were discharged alive, not transferred to another acute care hospital, and readmitted to any hospital within 30 days of discharge, consistent with the CMS publicly reported readmission measures.

Sample Characteristics

We examined the following characteristics of patients admitted for hyperglycemia and hypoglycemia in each year: age (65-74, 75-84, ≥85 years), sex, race (white, black, other), and the presence of 20 key comorbidities. We focused on comorbidities that are currently used to produce hospital risk-standardized 30-day mortality rates by the CMS for profiling hospital performance for myocardial infarction, heart failure, and pneumonia. We identified these comorbidities from secondary diagnosis codes recorded at the time of discharge from hospitalization for hyperglycemia and hypo-
glycemia as well as primary or secondary diagnosis codes of all inpatient hospitalizations up to 1 year before the index hospitalization.

Statistical Analysis
To analyze whether changes over time in the primary outcomes (hyperglycemia and hypoglycemia hospitalizations, mortality and readmission rates) were statistically significant, we used the Mantel-Haenszel χ² test. We also used this test in prespecified demographic subgroups (age, sex, and race).

To estimate the national trend in hyperglycemia and hypoglycemia hospitalization rates over time, we calculated the total number of hospitalizations and the total person-years in each state by year for 18 demographic combinations—representing 3 age categories (65-74, 75-84, and ≥85 years), 2 sex categories, and 3 race categories (white, black, other). We then fitted a generalized linear mixed-effects model with a Poisson link function, adjusting for age, sex, and race. The log-transformed total person-years value was used as an offset in the model to obtain the expected number of hospitalizations.

Using year 1999 as the baseline year, we included 12 dummy time variables, representing subsequent years from 2000 to 2011, to assess the trend in hospitalizations over the study period. To estimate the national trend in 1-year and 30-day mortality rates over time, we fitted a linear mixed-effects model to obtain the expected number of hospitalizations. The overall observed rate of hospitalization for hyperglycemia declined by 38.6% during this time period, from 114 to 70 hospitalizations per 100,000 person-years (Figure 1A, eTable 2 in the Supplement). The decline was steepest between 1999 and 2006; subsequently, hospitalizations for hyperglycemia increased slightly from 66 hospitalizations per 100,000 person-years in 2006 to 70 hospitalizations per 100,000 person-years in 2011. In analyses adjusted for age, race, and sex, the overall incidence risk ratio (IRR) for hyperglycemia was 0.62 (95% CI, 0.60-0.65) in 2011 relative to the baseline year 1999.

Results

Sample Characteristics
The final sample consisted of 33,952,331 unique individual Medicare beneficiaries 65 years or older who contributed a total of 363,261,068 person-years of observation from 1999 to 2011. Characteristics of patients hospitalized for hyperglycemia and hypoglycemia are reported in Table 1.

Hyperglycemia Hospitalization Trends
There were a total of 302,095 hospitalizations for hyperglycemia contributed by 279,937 beneficiaries from 1999 to 2011. The observed rate of hospitalization for hyperglycemia declined by 38.6% during this time period, from 114 to 70 hospitalizations per 100,000 person-years (Figure 1A, eTable 2 in the Supplement). The decline was steepest between 1999 and 2006; subsequently, hospitalizations for hyperglycemia increased slightly from 66 hospitalizations per 100,000 person-years in 2006 to 70 hospitalizations per 100,000 person-years in 2011. In analyses adjusted for age, race, and sex, the overall incidence risk ratio (IRR) for hyperglycemia was 0.62 (95% CI, 0.60-0.65) in 2011 relative to the baseline year 1999.

Hypoglycemia Hospitalization Trends
There were a total of 429,850 hospitalizations for hypoglycemia contributed by 404,467 beneficiaries from 1999 to 2011. The overall observed rate of hospitalization for hypoglycemia increased by 11.7% (from 94 to 105 hospitalizations per 100,000 person-years) during this time period (Figure 1A, eTable 2 in the Supplement). Admissions for hypoglycemia increased until 2007 (to 130 per 100,000 person-years), and declined subsequently, but remained above the baseline (1999) levels. In analyses adjusted for age, race, and sex, the overall IRR for hypoglycemia was 1.11 (95% CI, 1.08-1.13) for 2011 relative to the baseline year 1999.

Mortality and Readmission Trends
Among beneficiaries admitted for hyperglycemia, observed 30-day morality rates were 7.1% (95% CI, 6.8%-7.4%) in 1999 and 5.2% (95% CI, 4.9%-5.5%) in 2010, while 1-year mortality rates were 21.4% (95% CI, 21.0%-21.9%) in 1999 and 17.6% (95% CI,
Among patients admitted for hypoglycemia, the observed 30-day mortality rates were 5.0% (95% CI, 4.7%-5.2%) in 1999 and 5.0% (95% CI, 4.7%-5.2%) in 2010, while 1-year mortality rates were 23.3% (95% CI, 22.8%-23.9%) in 1999 and 22.6% (95% CI, 22.1%-23.0%) in 2010. Thirty-day readmission rates were 16.0% (95% CI, 15.5%-16.4%) in 1999 and 16.4% (95% CI, 15.8%-16.9%) in 2010 among patients admitted for hyperglycemia and 17.2% (95% CI, 16.8%-17.7%) in 1999 and 18.1% (95% CI, 17.6%-18.5%) in 2010 among patients admitted for hypoglycemia.

In risk-adjusted analyses, mortality and readmission outcomes after an index hospitalization for hyperglycemia and hypoglycemia improved during the study period. Adjusted ORs for 30-day and 1-year mortality in 2010 compared with baseline year 1999 were 0.75 (95% CI, 0.69-0.81) and 0.76 (95% CI, 0.72-0.80), respectively, among patients with hyperglycemia and 0.87 (95% CI, 0.81-0.95) and 0.82 (95% CI, 0.78-0.85), respectively, among patients with hypoglycemia. Adjusted ORs for 30-day readmission in 2010 compared with 1999 were 0.95 (95% CI, 0.90-1.00) and 0.93 (95% CI, 0.89-0.97) among beneficiaries with hyperglycemia and hypoglycemia, respectively. Risk-adjusted outcomes are shown in Table 2. We found no statistically significant interactions in trends of 30-day mortality, 1-year mortality, and 30-day readmission rates among age, sex, and racial subgroups for the hyperglycemia condition. We found significant interactions by race and age for readmission among patients with hypoglycemia. The effects of these interactions were small (−0.0004 to 0.018).

### Hospitalization Rates Stratified by Age, Sex, and Race
Hospitalization rates for both conditions were slightly higher among women than men (Figure 1B and C). Hospitalization rates for hypoglycemia were nearly 2-fold higher among older (≥75 years) vs younger (65-74 years) beneficiaries over the study period (Figure 1D-F). Finally, we observed clinically meaningful differences in admission rates for hyperglycemia and hypoglycemia by race over the entire study period (Figure 1G-I). Black patients had nearly 4-fold higher admission rates for hyperglycemia and hypoglycemia compared with white patients, and these differences persisted over time.
Trends in admission rates for hyperglycemia and hypoglycemia over time were qualitatively similar across all subgroups. However, we found statistically significant interactions in hospitalization rates for time and sex (both hyperglycemia and hypoglycemia), time and black race (hyperglycemia only), and time and age (both hyperglycemia and hypoglycemia). The effects of these interactions were small (0.009-0.027). \( P < .001 \) for all comparisons.

**Additional Analyses**

In analyses designed to account for trends in DM prevalence using BRFSS data, we found a decline in admission rates for both hyperglycemia and hypoglycemia hospitalizations. The estimated prevalence of DM among adults 65 years or older was 13.9% in 1999 and 18.8% in 2010. Estimated rates of admissions among Medicare beneficiaries with DM are shown in Figure 2. Admission rates for hyperglycemia and hypoglycemia decreased from 1999 to 2010 by 55.2% and 9.5%, respectively.

In analyses designed to account for changes in the use of hospital observation services, similar trends and patterns for hyperglycemia and hypoglycemia hospitalizations were observed when we restricted the outcome to hospitalizations with an LOS longer than 2 days compared with the primary analysis (eFigure A1 in the Supplement).

### Discussion

Between 1999 and 2011, as glycemic control in the US population with DM improved,\textsuperscript{17,18} hyperglycemic events requiring hospital admission declined among older adults, but severe hy-
Poglycemic events requiring hospitalization increased. Black patients experienced much higher rates of hospitalizations for both hyperglycemia and hypoglycemia compared with white patients throughout the 12-year period, while adults 75 years or older had higher rates of hypoglycemia leading to admission than those 65 to 74 years old. Estimated rates of admissions among older adults with DM using additional data from the BRFSS showed an even more dramatic decline in hyperglycemia hospitalizations but also a slight decrease in hypoglycemia hospitalizations over time. These results show considerable progress in reduction of admissions for hyperglycemia that has not been matched by similar advances in prevention of admissions for hypoglycemia.

Our study based on hospital admissions for short-term complications of DM suggests a differential effect of changes in DM treatment on rates of severe hyperglycemia and hypoglycemia and provides a strong argument for incorporating hypoglycemia into future assessments of DM quality measures. Over the past decade, DM care quality metrics have primarily rewarded target-based lowering of glucose levels\textsuperscript{4,15,17} based on evidence that persistent hypoglycemia, as assessed by elevated HbA$_1c$ level, is associated with the development and pro-

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**Figure 1. Observed Rates of Hospital Admissions for Hyperglycemia and Hypoglycemia, 1999 to 2011**

A, Overall. B and C, Among females and males, respectively. Among age subgroups: D, 65- to 74-year-olds; E, 75- to 84-year-olds; F, those 85 years or older. Among racial subgroups: G, black; H, other race/ethnicity; I, white. Note: To provide consistent axes for all relevant subgroups, the y-axis is on a logarithmic scale. The circles and diamonds indicate observed values; the lines represent the smoothed trend over time.

**Table 2. Risk-Adjusted Outcomes After Hospitalization for Hyperglycemia and Hypoglycemia, 1999 to 2010\textsuperscript{a,b}**

<table>
<thead>
<tr>
<th>Year</th>
<th>Reason for Hospitalization</th>
<th>1999</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
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<th>2005</th>
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<th>2008</th>
<th>2009</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperglycemia</td>
<td>Beneficiaries, No.</td>
<td>28104</td>
<td>27782</td>
<td>27589</td>
<td>26319</td>
<td>23591</td>
<td>21643</td>
<td>19961</td>
<td>17409</td>
<td>16934</td>
<td>17268</td>
<td>17387</td>
<td>17860</td>
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<tr>
<td></td>
<td>30-d Mortality, %</td>
<td>7.1</td>
<td>7.0</td>
<td>7.2</td>
<td>7.2</td>
<td>7.4</td>
<td>6.8</td>
<td>6.3</td>
<td>5.8</td>
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<td></td>
<td>1-y Mortality, %</td>
<td>21.4</td>
<td>21.4</td>
<td>21.6</td>
<td>20.9</td>
<td>20.7</td>
<td>19.7</td>
<td>18.3</td>
<td>18.3</td>
<td>17.9</td>
<td>17.5</td>
<td>17.1</td>
<td>17.1</td>
</tr>
<tr>
<td></td>
<td>30-d Readmission, %</td>
<td>16.0</td>
<td>15.7</td>
<td>16.0</td>
<td>15.6</td>
<td>15.7</td>
<td>16.1</td>
<td>16.3</td>
<td>15.9</td>
<td>15.6</td>
<td>15.9</td>
<td>15.7</td>
<td>15.3</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>Beneficiaries, No.</td>
<td>23630</td>
<td>26540</td>
<td>30548</td>
<td>32354</td>
<td>33575</td>
<td>34015</td>
<td>35056</td>
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<td>33732</td>
<td>32426</td>
<td>30341</td>
<td>30193</td>
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<td>30-d Mortality, %</td>
<td>5.0</td>
<td>5.0</td>
<td>5.1</td>
<td>4.8</td>
<td>4.7</td>
<td>4.3</td>
<td>4.3</td>
<td>3.8</td>
<td>4.1</td>
<td>4.6</td>
<td>4.4</td>
<td>4.4</td>
</tr>
<tr>
<td></td>
<td>1-y Mortality, %</td>
<td>23.3</td>
<td>22.9</td>
<td>23.3</td>
<td>21.7</td>
<td>21.3</td>
<td>19.9</td>
<td>19.4</td>
<td>18.4</td>
<td>19.4</td>
<td>19.8</td>
<td>20.5</td>
<td>19.9</td>
</tr>
<tr>
<td></td>
<td>30-d Readmission, %</td>
<td>17.3</td>
<td>17.9</td>
<td>17.4</td>
<td>17.2</td>
<td>16.7</td>
<td>16.7</td>
<td>16.4</td>
<td>16.0</td>
<td>16.1</td>
<td>16.3</td>
<td>16.3</td>
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\textsuperscript{a}Outcomes were risk-adjusted for demographics and all comorbidities and geriatric conditions presented in Table 1.

\textsuperscript{b}Data for mortality and readmissions were not available for hospitalizations in 2011 because we did not have access to follow-up data in 2012.
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between 1999 and 2010, a recent study evaluated DM care based on nationally representative snapshots of risk-factor control be-
tween 1999 and 2010, a recent study evaluated DM care based on nationally representative snapshots of risk-factor control and concluded that preventive practices and glycemic control have improved during the study period. In particular, the proportion of the population with DM meeting HbA1c target levels lower than 7% and lower than 8% increased from 1999 to 2002 and from 2003 to 2006, although it did not change significantly in the subsequent 2007-2010 period. Our data suggest that these improvements in glucose control were accompanied by a marked reduction in hyperglycemia among beneficiaries with DM, but a substantially smaller decline in hypoglycemia, a recognized harm associated with treatment.

The modest decline in hospital admissions for hyperglycemia after 2007 coincides with the well-publicized results from 3 large cardiovascular trials, published in 2008, each of which demonstrated no significant benefit on macrovascular outcomes from more intensive glycemic control. The ACCORD trial was terminated prematurely in early 2008 because of an unexpected increase in all-cause mortality in those patients assigned to the more aggressive strategy. These results led to a call for more moderated approaches to lowering of glucose levels by professional groups. The trends in our study may at least partly reflect overall secular trends in the intensity of glycemic control in older patients with type 2 DM subsequent to these trials. However, other changes in the treatment of patients with DM could have contributed as well, including greater use of medications that do not typically lead to hypoglycemia.

We found significant age and racial differences in rates of hospital admissions for hyperglycemia and hypoglycemia. Consistent with prior studies, admission rates for hypoglycemia were twice as high among older patients (≥75 years old) compared with younger patients (65-74 years old). A recent study based on National Electronic Injury Surveillance System project estimated an annual rate of emergency department visits for insulin-related hypoglycemia and errors to be 20.5 and 34.9 per 1000 insulin-treated patients with DM 65 years old and 80 years or older, respectively. These rate estimates are not directly comparable with ours because both the outcome and the denominator differ. Nevertheless, they confirm much higher rates of severe hypoglycemia among the oldest patients. Meal-planning misadventures and insulin product mix-ups were identified as potential reasons for these events. In addition, older patients may be more susceptible to hypoglycemia and its adverse consequences owing to aging-related changes in renal function, drug clearance, counter-regulatory responses, as well as cognitive dysfunction and highly prevalent polypharmacy.

In our study, admission rates for hyperglycemia and hypoglycemia were 4 times as high among black patients compared with white patients. Although DM disproportionately affects blacks, differences in the prevalence of DM would be expected to, at most, double these admissions. Prior studies have shown higher HbA1c levels among black patients compared with white patients, with a reduction in these differences after age 65 years when Medicare coverage becomes available. Higher HbA1c levels may be associated with uncontrolled or untreated DM and explain more frequent admissions for hyperglycemia among blacks. However, black patients also have higher rates of emergency department visits for hypoglycemia compared with white patients with DM. It is, therefore, possible that strategies focused primarily on intensifying glycemic control among black patients may potentially exacerbate disparities in hypoglycemia.

The short- and long-term mortality and readmission rates after hospitalization were similar for hyperglycemia and hypoglycemia, and both declined significantly over time. Improved monitoring, treatment, and coordination of care either during or after hospitalization may have contributed to these trends, or they may simply reflect secular trends in improved DM outcomes over time. Patients hospitalized for hypoglycemic events had a higher comorbidity burden compared with patients hospitalized for hyperglycemia. However, outcomes after hospital admission for either metabolic complication were
Admissions for Hyperglycemia and Hypoglycemia

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Author Contributions: Dr Wang had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Lipska, Minges, Huang, Gill, Krumholz.

Acquisition, analysis, or interpretation of data: Lipska, Ross, Wang, Inzucchi, Minges, Karter, Desai.

Drafting of the manuscript: Lipska.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Wang, Karter, Desai.

Obtained funding: Krumholz

Administrative, technical, or material support: Minges.

Study supervision: Inzucchi, Huang, Gill.

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