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The Risks and Benefits of Implementing Glycemic Control Guidelines in Frail Elders with Diabetes

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Abstract

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Employment or Affiliation		X		X		X		X		X		X
Grants/Funds		X		X		X		X		X		X
Honoraria		X		X		X		X		X		X
Speaker Forum		X		X		X		X		X		X
Consultant		X		X		X		X		X		X
Stocks		X		X		X		X		X		X
Royalties		X		X		X		X		X		X
Expert Testimony		X		X		X		X		X		X
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Author Contributions:

Dr. Lee designed the study, interpreted the data and wrote the manuscript.

Dr. Boscardin analyzed the data and provided critical revisions of the manuscript.

Ms. Cenzer provided statistical support.

Drs. Huang and Eng and Ms. Rice-Trumble provided critical revisions of the manuscript.

Ms. Rice-Trumble and Dr. Eng supported data collection and data cleaning.

Dr. Lee provided supervision in all phases of the study.

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BACKGROUND/OBJECTIVES—To determine the hypo- and hyper-glycemic outcomes associated with implementing the American Geriatrics Society (AGS) guideline for Hemoglobin A1c (HbA1c) <8% in frail older patients with diabetes.

DESIGN/SETTING—Guideline Implementation in PACE (Program of All-Inclusive Care for the Elderly)

PARTICIPANTS—All patients in the *Before* (10/02–12/04, n=338), *Early* (1/05–6/06, n=289) and *Late* phases of guideline implementation (7/06–12/08, n=385) with a diagnosis of diabetes mellitus and at least one HbA1c measurement.

INTERVENTION—Clinician education in 2005 with annual monitoring of the proportion of each clinician's patients with diabetes with HbA1c <8%.

MEASUREMENTS—Hypoglycemia (Blood sugar or BS <50), hyperglycemia (BS >400) and severe hypoglycemia (Emergency room or ER visit for hypoglycemia)

RESULTS—*Before*, *Early* and *Late* groups were similar in mean age, race/ethnicity, comorbidity and functional dependency. Antihyperglycemic medication use increased with more patients using metformin (28% *Before* versus 42% *Late*, $p < 0.001$) and insulin (23% *Before* versus 34% *Late*, $p < 0.001$), with more patients achieving the AGS glycemic target of HbA1c <8% (74% *Before* versus 84% *Late*, $p < 0.001$). Episodes of hyperglycemia (per 100 person-years) decreased dramatically (159 *Before* versus 46 *Late*, $p < 0.001$) and episodes of hypoglycemia were unchanged (10.1 versus 9.3, $p = 0.50$). Episodes of severe hypoglycemia were increased in the *Early* period (1.1 *Before* versus 2.9 *Early*, $p = 0.03$).

CONCLUSION—Implementing the AGS glycemic control guideline for frail elders led to fewer hyperglycemic episodes, but more severe hypoglycemic episodes requiring ER visits in the *Early* implementation period. Future glycemic control guideline implementation efforts should be coupled with close monitoring for severe hypoglycemia in the early implementation period.

Keywords

glycemic control; guideline; hypoglycemia; PACE; diabetes mellitus

INTRODUCTION

Glycemic control is a central element of care for all patients with Diabetes Mellitus (DM) and glycemic control targets have long been a focus of clinical practice guidelines. [1–3] After randomized trials suggested that more intensive glycemic control could decrease microvascular complications, [4, 5] the American Diabetes Association (ADA) recommended a target Hemoglobin A1c (HbA1c) <7%. [6] Although the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study results suggesting that tight glycemic control may be harmful for some patients have led to some loosening of these target HbA1c values, [7–9] glycemic control guidelines continue to encourage clinicians to intensify treatment and improve glycemic control for most patients with diabetes. [10]

While achieving these glycemic control targets may benefit a large proportion of the general population of patients living with diabetes, there is considerable uncertainty regarding the most appropriate glycemic targets for frail older patients. [11–18] The initial trials showing the benefits of tight glycemic control excluded older patients, [4, 5] making it unclear whether those results apply to the frail elderly. More recent trials that evaluated very intensive glycemic control such as ACCORD, ADVANCE (Action in Diabetes and Vascular Disease) and VADT (Veterans Affairs Diabetes Trial) have enrolled older patients, but found that the benefits were modest and in some cases, outweighed by the harms. [7, 19, 20]

Observational studies suggest that older patients with more comorbid conditions taking more medications are at higher risk for hypoglycemia than younger patients. [21, 22] Furthermore, because many of the benefits of more intensive glycemic control do not appear for many years, [23, 24] frail elders with limited life expectancy may receive little or no benefit from intensive glycemic control. Thus, recent guidelines acknowledge that the frail elderly may not benefit from intensive glycemic control [10, 25, 26] and in 2003, the California Healthcare Foundation/American Geriatrics Society (CHCF/AGS) Panel on Improving Care for Elders with Diabetes suggested that a HbA1c <8% may be most appropriate for frail elders. [14]

In 2004, the medical leadership at On Lok Senior Health recognized that over 30% of their frail older enrollees with diabetes had HbA1c >8% and thus did not meet the newly established glycemic control guideline. A program of clinician education and monitoring was initiated to decrease the proportion of patients with diabetes whose HbA1c >8%. First, a series of in-service presentations were provided to clinicians advising them of the many aspects of the CHCF/AGS guidelines on the care of older adults with diabetes, including the recommended glycemic control target for frail older patients. After these educational presentations, quality indicators were formulated, including an indicator showing the proportion of elders with diabetes with a HbA1c >8% for each clinician. A retrospective baseline report provided all clinicians with the proportion of their patients with diabetes whose HbA1c was >8% in the past year and this proportion was recalculated annually to provide ongoing feedback and monitoring.

To our knowledge, no studies have examined outcomes associated with implementing the glycemic control target recommended by the AGS guideline in a real-world population of frail, older patients with diabetes. Thus, our objective was to examine hypo- and hyperglycemic outcomes associated with the implementation of a guideline-recommended HbA1c target of 8% in frail older patients with diabetes. We compared rates of hypoglycemia, hyperglycemia, severe hypoglycemia requiring Emergency Room (ER) visits, HbA1c levels and antihyperglycemic medication use *Before* guideline implementation, during the *Early* period of guideline implementation and during the *Late* period of guideline implementation. Our overarching aim was to inform clinical leaders about the risks and benefits associated with implementing guideline-recommended glycemic control targets in frail older patients with diabetes.

METHODS

Participants and Guideline Implementation

We conducted a pre-/post- implementation study of On Lok Senior Health enrollees with diabetes mellitus from October 2002 (when an electronic medical record system was implemented) to December 2008. On Lok, the original model for Programs of All-Inclusive Care for the Elderly (PACE), requires enrollees to be 55 years and older and be certified by Medicaid as “nursing home eligible,” indicating that the participant requires ongoing skilled help and is thus unable to live independently. [27, 28] On Lok helps nursing home eligible enrollees remain in the community by providing transportation to health centers, where the following services are provided: meals, medications, bathing/showering, recreational activities, physical and occupational therapy, social work, nursing and physician services. Most On Lok enrollees are socioeconomically disadvantaged, with over 90% being dual-eligible and qualifying for both Medicaid and Medicare.

The educational intervention to increase the rates of guideline-concordant glycemic control was targeted toward 21 salaried On Lok clinicians, initiated in 2005 and ran through the first half of 2006. Thus, we divided our study into three periods: the *Before* period (Oct 2002 –

Dec 2004), the *Early* implementation period (Jan 2005 – Jun 2006) and the *Late* Implementation period (Jul 2006 – Dec 2008), and compared outcomes between the three time periods. Participants were considered diabetic and included in the study if they had a diagnosis of diabetes mellitus (ICD9: 250.xx) and a HbA1c value during the study period. After excluding enrollees from each period if they had missing functional assessments (n=20), our study population included 338 enrollees in the *Before* period, 289 enrollees in the *Early* period and 385 enrollees in the *Late* period.

Because our goal was to examine the real-world effects of implementing glycemic control guidelines, our study population mirrored most practice populations and was dynamic, non-independent and at steady-state. First, in most clinical settings, the patient population is dynamic with different patients entering, leaving and remaining in the practice. To mirror this in our study, we examined all On Lok enrollees during the study period, including those that entered On Lok after study inception (Oct 2002) and those that died or disenrolled from On Lok before study conclusion (Dec 2008). Second, our comparison groups were non-independent, with many enrollees contributing data to more than one time period (e.g. *Before* and *Early*) if they had a HbA1c value obtained in multiple time periods. Thus, 70% of the enrollees in the *Early* period also contributed to the *Before* period, and 41% of the enrollees in the *Late* period also contributed to the *Before* period. Third, our study population was at steady-state, with On Lok maintaining its census throughout our study. Thus, despite the dynamic nature of our study population, at study conclusion, our population was similar in age and other factors compared to our population at study inception. Although our complex study population necessitated more sophisticated statistical methods, our study design most closely resembles real-world clinical populations and thus most effectively informs clinical leaders of the likely results of implementing guideline-recommended glycemic control targets.

Measures: Outcomes

Primary outcomes were the episodes of hypoglycemia, hyperglycemia and hypoglycemia-related emergency room visits. Episodes of hypoglycemia were defined as blood glucose measurements <50 and episodes of hyperglycemia were defined as blood glucose measurements >400. All point-of-care fingerstick glucose measurements and laboratory glucose measurements were captured in the electronic medical record during the study period. Fingerstick glucose was measured to comply with a standing physician order or when the patient exhibited symptoms concerning for hypo- or hyper- glycemia. To determine whether there was increased blood glucose testing across our study period, we calculated the total number of blood glucose measurement per patient per month for each of the time periods. We found that rates of blood glucose measurements declined slightly across the three time periods, suggesting that the guideline implementation did not lead to more frequent blood glucose measurements. Hypoglycemia-related ER visits were identified through ER principal diagnosis ICD-9 codes (249.8x, 250.8x, 251.0, 251.1, 251.2). We also examined hyperglycemia-related ER visits but found only 1 episode during our entire study period; thus, we did not consider hyperglycemia-related ER visits further.

Secondary outcomes included antihyperglycemic medication use and HbA1c levels. Since On Lok provides a prescription drug benefit, all medications are dispensed through one contract pharmacy resulting in complete medication records. We categorized antihyperglycemic medications into insulin (e.g. Regular, NPH and glargine), sulfonylurea (e.g. glyburide and glimepiride), metformin thiazolidinediones (e.g. pioglitazone and rosiglitazone) and other (e.g. acarbose). We examined the medication list on the date of each enrollee's first HbA1c measurement in the *Before*, *Early* or *Late* time periods. For HbA1c levels, we averaged all HbA1c values for a given enrollee in each time period.

Measures: Predictors and Confounding Variables

Our primary predictor variable was the time period: *Before*, *Early* implementation or *Late* implementation. The age of individual participants was determined at their entry into each time period. [29] Functional dependencies were determined through quarterly interdisciplinary evaluations involving nursing, physical and occupational therapy, medicine and social work. Activities of Daily Living or ADL (bathing, toileting, transferring, eating, dressing and walking across a room) were categorized as independent, partially dependent or fully dependent. Comorbid conditions were captured through ICD9 codes associated with hospitalizations, Emergency Room (ER) visits and outpatient physician visits. We based our ICD9 codes on a published synthesis of the Charlson-Deyo and Elixhauser algorithms [30] to identify participants with chronic obstructive pulmonary disease or COPD (416.8, 416.9, 490.x – 505.x, 506.4, 508.1, 508.8), congestive heart failure or CHF (398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4 – 425.9, 428.x), cancer (140.x – 172.x, 174.x – 195.8, 196.x – 199.x, 200.x – 208.x, 238.6) and kidney disease (403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582.x, 583.0 – 583.7, 585, 585.5, 585.6, 586.x, 588.0, V42.0, V45.1, V56.x).

Statistical Analysis

We compared the baseline characteristics, medications and HbA1c values between the *Before* and *Early* groups and between the *Before* and *Late* groups. We used bootstrap samples to determine whether differences between the groups were statistically significant (500 repetitions). To account for the non-independence of our samples with some enrollees contributing data to both the *Before* and *Early/Late* groups, we sampled at the subject level. Thus, if an enrollee was included in a bootstrap sample of the *Before* cohort and that enrollee was also in the *Early* cohort, that enrollee would also be included in the comparison bootstrap sample of the *Early* cohort.

To determine whether the rates of primary outcomes differed between time periods, we used a mixed effects Poisson regression using counts of our outcomes over time, with 3-month intervals (quarters) as fixed effects (starting with the 4th quarter of 2002 and ending with 4th quarter of 2008) and a random intercept for each subject. This allowed us to model a unique trajectory for each enrollee, which varied around the trajectory described by the model's overall fixed effects. We included the time periods (*Before*, *Early* and *Late*) as a covariate, to determine whether the outcome rates varied significantly between the periods. We also adjusted for a mortality index developed for the PACE population, which included age, gender, functional dependencies and comorbidities. [29] As a sensitivity analysis, we restricted our sample to participants who were enrolled in all three periods. Since our results were similar, we present our primary analysis of all enrollees. As a further sensitivity analysis and to verify the validity of our mixed effects Poisson model, we fit Generalized Estimating Equation (GEE) models, using both Poisson and negative binomial regressions. Since the results were similar, we present our primary mixed effects Poisson regression results.

To determine the rate of hypoglycemia for various antihyperglycemic drugs, we calculated the total number of episodes that occurred while patients were taking drug X and divided it by the total person-years of exposure of all patients to drug X. To calculate the risk ratio for hypoglycemia between antihyperglycemic drugs, we bootstrapped at the subject level, allowing us to determine 1) the standard errors for the rates of hypoglycemia by antihyperglycemic drug and 2) confidence intervals for risk ratios between antihyperglycemic drugs. We separated age from the PACE mortality index [29] to determine whether age was associated with hypoglycemia. Due to the small number of severe hypoglycemia episodes requiring ER visits, we focused on episodes of hypoglycemia.

All statistics were performed using Stata MP (version 10.1; StataCorp 2007, College Station, TX) and SAS (Version 9.2, SAS System for Windows, 2008, SAS Institute Inc, Cary, NC). The Committee on Human Research of the University of California, San Francisco and the San Francisco Veterans Affairs Research and Development committee approved this study.

RESULTS

Characteristics of the Participants

Study participants were generally similar across the *Before*, *Early* and *Late* time periods, with similar mean age, gender and race and ethnicity. (Table 1) The *Late* group had fewer enrollees with congestive heart failure (29% vs 34% in the *Before* group, $p=0.03$) but the proportion of enrollees with chronic obstructive pulmonary disease, cancer and kidney disease were similar between the *Before* and *Late* groups. Participants were frail across the three study time periods, with over 60% dependent in at least 2 ADLs. There were no differences across all factors (demographic, comorbid conditions and functional dependencies) between the *Before* and *Early* groups.

Increased Intensity of Treatment and Lower Hemoglobin A1c Levels

Study participants received more intensive antihyperglycemic regimens in the *Late* implementation period compared to the *Before* period. (Table 2) The number of enrollees with diabetes who were not taking any antihyperglycemic medications dropped from 40% in the *Before* period to 33% in the *Late* period ($p=0.03$), suggesting that the improved rates of glycemic control was not due to an increase in the prevalence of milder cases of diabetes. Forty-two percent of enrollees with diabetes in the *Late* period were taking Metformin compared to 28% of enrollees with diabetes in the *Before* period ($p<0.001$), with little difference between enrollees >80 and <80 years of age. Twenty percent of enrollees were taking thiazolidinediones or other antihyperglycemic medications in the *Late* period compared to 7% in the *Before* period ($p<0.001$). Thirty-four percent of enrollees were taking insulin in the *Late* period compared to 23% in the *Before* period ($p<0.001$).

Patients with diabetes in the *Early* implementation period had treatment regimens that were intermediate in intensity compared to patients in the *Before* and *Late* periods, with intermediate rates of insulin and thiazolidinedione or other hyperglycemic medication use. However, the rates of sulfonylurea use was decreased compared to the *Before* period (38% vs 49%, $p<0.001$).

The increased intensity of treatment in the *Late* implementation period was associated with lower HbA1c levels. (Table 3) Forty-six percent of participants had an HbA1c $<7\%$ in the *Before* period compared to 57% of participants in the *Late* period ($p=0.001$). Seventy-four percent of participants achieved the guideline-recommended goal of HbA1c $<8\%$ in the *Before* period, compared to 84% of participants in the *Late* period ($p=0.001$). Mean HbA1c dropped from 7.4 in the *Before* period to 7.0 in the *Late* period ($p<0.001$). The *Early* implementation period was again intermediate between the *Before* and *Late* periods, with 46% of participants with an HbA1c $<7\%$ and 75% of participants with an A1c $<8\%$.

Episodes of Hypoglycemia, Hyperglycemia and Hypoglycemic-Related Emergency Room Visits

Episodes of hyperglycemia decreased dramatically from the *Before* to *Late* implementation periods, going from 159 episodes per 100 person-years to 46 episodes ($p < 0.001$). (Table 4) In contrast, episodes of hypoglycemia were similar between the *Before* and *Late* periods, with 10.1 episodes per 100 person-years in the *Before* period and 9.3 episodes in the *Late* period ($p=0.43$). Hypoglycemia-related ER visits occurred more frequently in the *Early*

implementation period, rising from a rate of 1.1 visits per 100 person-years in the *Before* period to 2.9 visits in the *Early* period ($p=0.03$). In the *Late* period, the rate of ER visits decreased to 0.63 ($p=0.88$ compared to *Before*).

Our multivariate adjusted mixed effects Poisson models suggested that that risk of a hyperglycemic episode was 53% less in the *Late* implementation period compared to the *Before* period (95% CI: 46% to 60%). The risk of a hyperglycemic episode was also decreased 22% in the *Early* implementation period compared to the *Before* period (95% CI: 12% to 32%). The risk of a hypoglycemic episode was unchanged between the *Before*, *Early* and *Late* periods. The risk of a hypoglycemia-related ER visit was increased in the *Early* period compared to the *Before* period with a 203% increase (95% CI: 17% to 682%). The risk of a hypoglycemia related ER visit was similar between the *Before* and *Late* periods.

We further explored the episodes of severe hypoglycemia requiring ER visits in the *Early* period to better characterize this high risk group. Nine participants suffered a total of 13 episodes of hypoglycemia requiring ER visits in the *Early* period. All of these participants remained alive, enrolled in On Lok and included in our *Late* period study population, making it unlikely that the decrease in episodes of hypoglycemia requiring ER visits in the *Late* period was due to participants predisposed to hypoglycemia leaving On Lok and our study. Eight of 9 participants had episodes of hyperglycemia in the months preceding hypoglycemia, suggesting that these participants were “brittle,” with widely fluctuating blood glucose measurements.

Risk Factors for Hypoglycemia

Our analysis for the risk factors for hypoglycemia showed that insulin use was associated with an increased risk of hypoglycemia compared to Metformin (Rate ratio 2.16, 95% CI: 1.28 – 3.04). (Table 5) Metformin and Sulfonyleureas were associated with the lowest risk of hypoglycemia (9.8 and 9.4, respectively). Thiazolidinediones were intermediate between insulin and metformin in hypoglycemia risk. Age was not associated with hypoglycemia ($p=0.55$).

DISCUSSION

We found that intensifying the antihyperglycemic medication regimen to meet a guideline-recommended threshold for glycemic control in frail, nursing-home eligible elders with diabetes was effective and associated with both positive and negative outcomes. After guideline implementation, we observed increases in the rates of insulin and oral antihyperglycemic medication use several times greater than the changes seen in national trends. [31] The increased intensity of treatment resulted in lower mean HbA1c levels and fewer participants with HbA1c levels greater than the recommended target of 8%. This improvement in glycemic control was associated with a dramatic reduction in episodes of hyperglycemia, with a 54% decreased risk of hyperglycemic episodes in the *Late* implementation period compared to the *Before* period. This decrease in the rate of hyperglycemic episodes between the *Before* and *Late* periods was not associated with an appreciable change in the rate of hypoglycemic episodes. However, the risk of severe hypoglycemia requiring ER visit appeared highest in the *Early* implementation period as new medications are being started. Insulin appears to be associated with higher risk of hypoglycemia than other antihyperglycemic agents.

Because the PACE model allows older, frail enrollees to be monitored closely, it may represent an ideal setting for intensifying glycemic control where the harms of hypoglycemia can be minimized. Most On Lok enrollees are observed by staff several times a week at the health center. Meals and recreational activities are provided, allowing

providers to get objective information about enrollees' diet and physical activity. Physicians and nurses are onsite, making it easier for enrollees to be evaluated frequently. Conversely, most frail elders not enrolled in PACE programs would receive care at outpatient clinics, where the frequency of interactions and the information available to clinicians would generally be more limited. However, even in the PACE setting with its inherent advantages, we found that intensifying glycemic control to meet the target of A1c <8% led to an increase in episodes of severe hypoglycemia requiring an ER visit. Thus, in usual clinic settings where such frequent monitoring is not feasible, our results suggest that implementing a HbA1c target of 8% in frail elders with diabetes may lead to increases in severe hypoglycemia and that a less stringent HbA1c target may be more appropriate.

Our results suggest that glycemic control guideline implementation may lead to a higher risk of severe hypoglycemic episodes requiring ER visits, but that this risk declines over time. One explanation for our findings is that there are a small number of patients with "brittle" diabetes who are at high risk for severe hypoglycemia. [32] When guideline implementation encourages treatment intensification, patients with "brittle" diabetes may have severe hypoglycemia even with a modest intensification of treatment. [33] Once these patients have an episode of severe hypoglycemia and are identified, they may be treated more liberally, and the rest of the population may be able to be treated more aggressively with fewer overall episodes of severe hypoglycemia.

Our results reinforce the critical importance of context and environment in guideline implementation. Systematic reviews have suggested that changing provider behavior is difficult and that the effect of education, feedback and monitoring are usually modest. [34–36] However, there is striking variation, with some studies reporting strong effects (up to 70% increase in compliance) and other studies reporting no effects. [34] Because On Lok is a small, closed system, with salaried clinicians and modest provider turnover (~5% per year), the education, feedback and monitoring appears to have resulted in significant changes in provider behavior.

Our results show that good guidelines sometimes do not make good quality indicators. [37, 38] Guidelines, such as the AGS diabetes guideline, provide guidance and are inherently flexible, allowing clinicians to incorporate clinical judgment and patient preferences to deliver ideal, individualized care. [37–41] Quality indicators, such as the one described in this study, strive to judge quality as adequate (or not) based on whether the indicator was met, and are thus inherently rigid. [37–41] Because of these differences, guidelines are better suited to highlight ideal care which may not be possible in all patients whereas quality indicators are better suited to focus on a basic standard of care which, when "not met, almost certainly identifies poor quality care." [41] Until recently, these important differences were not widely appreciated, contributing to the decision in 2007 by the National Committee on Quality Assurance (NCQA) to translate the ADA glycemic control guideline for adults (HbA1c <7%) into a Healthcare Effectiveness Data and Information Set (HEDIS) quality indicator. [39] In 2009, the NCQA restricted the use of the HbA1c <7% HEDIS indicator to younger, healthier patients and initiated a second quality indicator of HbA1c <8% for all adult patients, while the ADA reiterated its support for the guideline target of HbA1c <7%. [8, 42] The different glycemic targets between the ADA guidelines and the HEDIS quality indicators are appropriate and underscore a growing appreciation of the important differences between guidelines and quality indicators.

Our study has both strengths and limitations. The major strength of our study is that although previous studies have examined outcomes associated with improving glycemic control, [43] to our knowledge, our study is the first to focus on community dwelling frail elderly who are at higher risk for hypoglycemia due to polypharmacy and multimorbidity.

Our study also has several limitations. First, because patients and families must choose to enroll in PACE programs and elders who choose to enroll are likely different from elders who do not enroll. However, much of what is known about the frail elderly is based on nursing home populations, even though more elders who are eligible for nursing home care live in the community. [44] Thus, this is one of the first studies examining glycemic outcomes in an understudied, vulnerable population. Second, our Pre/Post study design is subject to biases due to temporal changes. However, similarities between the baseline characteristics of participants in the three time periods and the overall plausibility of our findings (intervention to improve glycemic control leading to increased antihyperglycemic medications, leading to decreased A1c levels, leading to decreased episodes of hyperglycemia) makes it less likely that biases completely explain our findings. Third, we did not have renal function data, which may have important associations with antihyperglycemic agents and hypoglycemia risk. However, it is unlikely that these relationship would differ across our three time periods, making it unlikely that renal function would account for our findings.

In conclusion, we found that guideline implementation to improve glycemic control to the recommended level of HbA1c <8% in frail, nursing home eligible community-dwelling elders led to increased use of antihyperglycemic medications, lower A1c levels and fewer episodes of hyperglycemia. However, there was a significant increase in the rates of severe hypoglycemia requiring ER visits in the *Early* implementation period, suggesting that future guideline implementation efforts should be coupled with close monitoring for hypoglycemia immediately following guideline implementation.

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Table 1

Characteristics of Participants

	Before (Oct 02 – Dec 04) (n=338)	Early (Jan 05 – Jun 06) (n=289)	Late (Jul 06 – Dec 08) (n=385)
Mean Age ± SD	79.8 ± 8.6	80.1 ± 8.6	79.7 ± 8.8
Male, (%)	99 (29)	91 (31)	132 (34)
Race/Ethnicity (%)			
White	43 (13)	36 (12)	49 (13)
African-American	32 (9)	24 (8)	26 (7)
Hispanic	39 (12)	36 (12)	56 (15)
Asian	224 (66)	193 (67)	254 (66)
Comorbidities (%)			
COPD	64 (19)	64 (22)	78 (20)
CHF	114 (34)	106 (37)	111 (29)*
Cancer	27 (8)	27 (9)	35 (9)
Kidney Disease	38 (11)	37 (13)	34 (9)
ADL Dependence (%)			
0	42 (12)	49 (17)	67 (17)
1	76 (22)	64 (22)	49 (13)
2–3	73 (23)	62 (21)	93 (24)
4–5	53 (16)	50 (17)	82 (21)
6–7	89 (26)	64 (22)	94 (24)

*
p<0.05, compared to *Before*

Table 2

Intensity of Diabetes Medication Treatment

	Before (%)	Early (%)	Late (%)
No Medications	136 (40)	131 (45)	126 (33) *
1 Oral Medication	124 (37)	98 (34)	130 (34)
2+ Oral Medications	78 (23)	60 (21)	129 (34) **
Metformin	93 (28)	80 (28)	162 (42) ***
Sulfonylureas	165 (49)	109 (38) ***	176 (46)
Thiazolidinediones and Other Antihyperglycemic Medications	25 (7)	35 (12) *	76 (20) ***
Insulin	77 (23)	75 (26)	131 (34) ***

*
p<0.05, compared to *Before*

**
p<0.01, compared to *Before*

p<0.001, compared to *Before*

Table 3

Average Hemoglobin A1c

A1c	Before (%)	Early (%)	Late (%)
<7	156 (46)	132 (46)	220 (57) **
7–7.9	94 (28)	85 (29)	103 (27)
8–8.9	41 (12)	38 (13)	37 (10)
9+	47 (14)	34 (12)	25 (6) **
Mean A1c ± SD	7.4 ± 1.5	7.4 ± 1.4	7.0 ± 1.1 ***

*
p<0.05, compared to *Before*

**
p<0.01, compared to *Before*

p<0.001, compared to *Before*

A1c categories are based on average A1c values for each individual in the *Before*, *Early* and *Late* time periods.

Table 4

Episodes of Hypoglycemia, Hyperglycemia and Hypoglycemia Requiring Emergency Room Visit Across Time Periods

	Before	Early	Late
Hypoglycemia			
Episodes per 100 Person-Years	10.1	9.8	9.3
Unadjusted Rate Ratio	--	0.96	(0.58, 1.25)
Compared to Before (95% CI)		(0.64, 1.43)	(0.58, 1.25)
Adjusted Rate Ratio Compared	--	0.96	0.86
to Before (95% CI)		(0.63, 1.46)	(0.58, 1.26)
Hyperglycemia			
Episodes per 100 Person-Years	158.8	89.0	45.5
Unadjusted Rate Ratio	--	0.80	0.47
Compared to Before (95% CI)		(0.70, 0.90)	(0.41, 0.55)
Adjusted Rate Ratio Compared	--	0.78	0.47
to Before (95% CI)		(0.68, 0.88)	(0.40, 0.54)
Hypoglycemia Requiring Emergency Room Visit			
Episodes per 100 Person-Years	1.1	2.9	0.63
Unadjusted Rate Ratio	--	2.80	0.64
Compared to Before (95% CI)		(1.08, 7.17)	(0.19, 2.12)
Adjusted Rate Ratio Compared	--	3.03	0.65
to Before (95% CI)		(1.17, 7.82)	(0.20, 2.14)

Adjusted Rate Ratio accounted for Mortality Index (age, gender, comorbid conditions and function dependencies) [29]

Table 5

Risk for Hypoglycemia with Different Medications

Medication	Rate of Hypoglycemia per 100 person-years	Rate Ratio (Ref = Metformin)
Metformin	9.8 ± 2.3	-
Sulfonylureas	9.4 ± 1.7	0.96 (0.49, 1.43)
Thiazolidinediones	13.2 ± 3.4	1.35 (0.63, 2.08)
Insulin	21.1 ± 3.8	2.16 (1.28, 3.04)