

# Glycosylated Hemoglobin and Functional Decline in Community-Dwelling Nursing Home–Eligible Elderly Adults with Diabetes Mellitus

Celia K. Yau, MD,\* Catherine Eng, MD,<sup>†‡</sup> Irena Stijacic Cenzer, MA,<sup>‡§</sup> W. John Boscardin, PhD,<sup>‡§</sup> Kathy Rice-Trumble, RN,<sup>†</sup> and Sei J. Lee, MD, MAS<sup>‡§</sup>

**OBJECTIVES:** To determine whether glycosylated hemoglobin (HbA1c) levels predict functional decline in older adults.

**DESIGN:** Longitudinal cohort study.

**PARTICIPANTS:** Community-dwelling, nursing home (NH)-eligible individuals with diabetes mellitus enrolled at On Lok between October 2002 and December 2008 (367 participants, 1,579 HbA1c measurements).

**SETTING:** On Lok Lifeways, the original model for Programs of All-Inclusive Care for the Elderly.

**MEASUREMENTS:** The outcomes were functional decline or death at 2 years. The primary predictor was HbA1c. Age, sex, race and ethnicity, baseline function, comorbid conditions, length of time enrolled at On Lok, insulin use, and clustering of HbA1c within participants were adjusted for with mixed-effects Poisson regression.

**RESULTS:** Mean age was 80, and 185 participants (50%) were taking insulin. Sixty-three percent of participants experienced functional decline, and 75% experienced death or functional decline during the study period. At 2 years, higher HbA1c was associated with less functional decline or death ( $P$  for trend = .006). Accounting for clustering and confounding factors, HbA1c of 8.0% to 8.9% was associated with a lower likelihood (relative risk = 0.88, 95% confidence interval = 0.79–0.99) of functional decline or death than HbA1c of 7.0% to 7.9%.

**CONCLUSION:** In community-dwelling, NH-eligible individuals with diabetes mellitus, HbA1c of 8.0% to 8.9% is associated with better functional outcomes at 2 years than HbA1c of 7.0% to 7.9%, suggesting that the current American Geriatrics Society guideline recommending a HbA1c target of 8.0% or less for older adults with

limited life expectancy may be lower than necessary to maintain function. *J Am Geriatr Soc* 60:1215–1221, 2012.

**Key words:** glycemic control; functional decline; hemoglobin A1c

Diabetes mellitus is common in older Americans and is strongly associated with disability and functional decline. In 2004, an estimated 324,000 Americans with diabetes mellitus were living in nursing homes (NH),<sup>1</sup> and a similar number of NH-eligible elderly adults with diabetes mellitus lived in the community with formal and informal caregiver support.<sup>2</sup> This growing population of older adults with diabetes mellitus has twice the risk of disability and functional decline of older adults without diabetes mellitus.<sup>3–5</sup> The greater risk of functional decline is especially important in older adults because function has been shown to be strongly associated with outcomes such as health-related quality of life,<sup>6,7</sup> NH placement, mortality, and cost.<sup>8,9</sup>

Although the presence of diabetes mellitus appears to be a strong risk factor for functional decline, it is unclear whether level of glycemic control affects functional outcomes. Poor glycemic control may lead to worsening neuropathy, malaise, urinary incontinence, and malnutrition, leading to functional decline.<sup>10</sup> Conversely, tight glycemic control may lead to more-frequent hypoglycemia or falls, leading to functional decline.<sup>11–15</sup> Thus, tight and poor glycemic control may lead to functional decline, but it is unknown whether any association exists in NH-eligible elderly adults who are at highest risk for functional decline. Determining the level of glycemic control associated with the best functional outcomes would help providers determine the most-appropriate glycemic target for older adults with diabetes mellitus.

Thus, the relationship between glycosylated hemoglobin (HbA1c) levels and 2-year functional decline was examined in community-dwelling, NH-eligible older adults

From the \*San Francisco VA PRIME Program, University of California at San Francisco, San Francisco, California; <sup>†</sup>On Lok Lifeways, San Francisco, California; <sup>‡</sup>Division of Geriatrics, University of California at San Francisco, San Francisco, California; and <sup>§</sup>San Francisco VA Research Enhancement Award Program, San Francisco, California.

Address correspondence to Sei J. Lee, 4150 Clement Street, Bldg 1, Rm 220F, San Francisco, CA 94121. E-mail: Sei.lee@ucsf.edu

DOI: 10.1111/j.1532-5415.2012.04041.x

with diabetes mellitus enrolled at On Lok Lifeways, the original model for Programs of All-Inclusive Care for the Elderly (PACE). It was hypothesized that PACE enrollees with diabetes mellitus who were able to achieve the American Geriatrics Society (AGS) recommended HbA1c target of 8.0% or lower<sup>16</sup> would have less functional decline than those whose HbA1c was greater than 8.0%.

## METHODS

### Participants

A longitudinal cohort study was conducted using repeated measures of glycemic control and functional decline in On Lok enrollees with diabetes mellitus between October 2002 (when an electronic medical record system was implemented) and December 2008. On Lok, the original model for the PACE program, requires enrollees to be certified as "NH-eligible," indicating that the participant requires ongoing skilled help and is unable to live independently.<sup>17,18</sup> On Lok helps NH-eligible enrollees remain in the community by providing and coordinating all health-care services, including primary and specialist physician services, adult day health care, home care, acute and post-acute hospitalization, and custodial NH care for those who require it. Enrollees receive health services in PACE centers that comprise co-located adult day health centers and medical clinics. The program provides participants with transportation to PACE centers, where meals; medication management; help with bathing and showering; recreational activities; physical and occupational therapy; and social work, nursing, and physician services are provided. Each enrollee receives a comprehensive health assessment upon enrollment and every 6 months thereafter. These assessments include medical evaluations and functional assessments performed by nurses, occupational therapists, and physical therapists.

Participants were included in the study if they were enrolled in On Lok at the start of the study period or entered On Lok between October 2002 and December 2006 (allowing for 24 months of follow-up), had a diagnosis of diabetes mellitus identified according to *International Classification of Diseases, Ninth Revision* (ICD-9), code (250.xx), and had at least one HbA1c value measured between October 2002 and December 2006 (464 participants with 2,144 HbA1c measurements). Because enrollment at On Lok is often associated with medication and functional changes, HbA1c measurements were excluded if they were collected less than 30 days after initial enrollment (159 measurements excluded) or if corresponding baseline functional assessments were collected less than 30 days after initial enrollment (116 measurements excluded). HbA1c measurements were also excluded if functional data were unavailable because there was no baseline functional assessment within 6 months before the HbA1c measurement (64 measurements excluded), the enrollee was disenrolled before the 24-month follow-up (100 measurements), or follow-up functional data were missing (75 measurements). Finally, measurements were excluded if participants were enrolled in end-of-life care (ICD-9: V66.7) (51 measurements excluded), leaving a final analytical cohort of 1,579 HbA1c measurements from 367 enrollees.

### Measures: Outcomes

The primary outcomes of the study were functional decline and functional decline or death within 2 years. Functional decline was defined as a decline in activity of daily living (ADL) score at follow-up from baseline. ADL score (range 0–10) was determined by combining each enrollee's level of functioning in five basic ADLs (bathing, dressing, toileting, transferring and eating) as independent (2 points), partially dependent (1 point), or completely dependent (0 points). Baseline ADL score was defined as the closest ADL score within 6 months before the HbA1c measurement, and the follow-up ADL score was defined as the ADL measurement  $24 \pm 3$  months after the HbA1c measurement. For participants who died within the 24-month follow-up period, functional decline was determined by comparing their baseline and last ADL scores before death.

Because the ADL assessments occurred every 6 months, participants who had less than 6 months of functional decline before death might have been missed using the definition of functional decline, so the outcome of functional decline or death within 24 months was also examined. As intermediate outcomes, functional decline or death was also examined at 6 and 12 months.

### Measures: Predictors and Confounding Variables

The primary predictor was HbA1c level divided into four categories (<7.0%, 7.0–7.9%, 8.0–8.9%, and  $\geq 9.0\%$ ). HbA1c was categorized because previous studies suggest that the relationship between HbA1c and outcomes may be nonlinear.<sup>19</sup> To characterize how HbA1c levels changed during follow-up, baseline HbA1c levels were compared with the last HbA1c measurement before 2-year follow-up or death.

Factors that may confound the relationship between HbA1c and functional status were accounted for, including sex and race or ethnicity. Age, length of time at On Lok, and use of oral antihyperglycemic medications or insulin was determined at each HbA1c measurement. Baseline function was defined as baseline ADL score. Because individuals requiring insulin may differ in complex ways from individuals taking oral medications and prior studies suggest that insulin use is associated with higher risk of physical disability,<sup>3,20</sup> analyses were performed stratified according to treatment (any insulin vs oral antihyperglycemic medications only) to determine whether the relationship between HbA1c and functional decline differed according to treatment. For the nonstratified analyses, treatment was included as a confounding factor. Because a previous study showed that an educational intervention in 2005 was successful in changing glycemic control practices at On Lok, year was accounted for in the analysis.<sup>21</sup> Comorbid conditions were captured through ICD-9 codes associated with hospitalizations, emergency department visits, and outpatient physician visits.

### Statistical Analysis

The unit of analysis was HbA1c measure (predictor) and 2-year death or functional decline (outcome).

A population-averaged mixed-effects Poisson regression was used to account for clustering of HbA1c values according to participant. Poisson regression was chosen over logistic regression because the outcome was common, making odds ratios more difficult to interpret than risk ratios. A HbA1c level of 7.0% to 7.9% was chosen as the reference because the AGS guideline recommends HbA1c of 8.0% or less as the appropriate glycemic target for “frail elders with limited life expectancy”<sup>16</sup> and was consistent with On Lok practices during the study period. The statistical significance of trends was tested by examining whether the slope of the outcome–HbA1c regression line from the unadjusted mixed-effects model differed from zero. As a sensitivity analysis, all participants who disenrolled were categorized as having functional decline and it was found that the results were unchanged.

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

## RESULTS

### Characteristics of the Participants

Table 1 shows baseline characteristics of the 367 participants and their 1,579 HbA1c measurements. Participants were elderly, with a mean age of 80, and most were female (67%) and Asian (65%). Almost one-third were taking only oral antihyperglycemic medications at baseline, and half were taking insulin. Most participants had functional limitations, with 66% of enrollees having a baseline ADL score of 8 or less. Most participants also showed evidence of cognitive impairment, with 79% of enrollees having a Short Portable Mental Status Questionnaire score of 6 or less. The most common oral antihyperglycemic medications were sulfonylureas (e.g., glipizide) (51% of participants) and biguanides (e.g., metformin) (40% participants). Of 367 participants, 231 (63%) had a decline in functional status, and 275 (75%) died or had a decline in functional status during the study period.

### Relationship Between HbA1c, Functional Decline, and Death

Figure 1 shows the unadjusted results at 6, 12, and 24 months. Twenty percent to 30% of participants in each HbA1c level in the cohort died by 2 years, confirming that the study population was at high risk for adverse outcomes. At 6 months, no clear association was seen between HbA1c level and the composite outcome of functional decline or death ( $P$ -value for trend = .44) (Figure 1). At 12 months, each higher level of HbA1c appeared to be associated with a lower rate of functional decline or death, although this trend was not statistically significant ( $P$ -value for trend = .24). By 2 years, higher HbA1c was associated with less functional decline or death, ( $P$ -value for trend = .006).

After 2 years of follow-up, functional decline was identified after 49% of HbA1c measurements, death

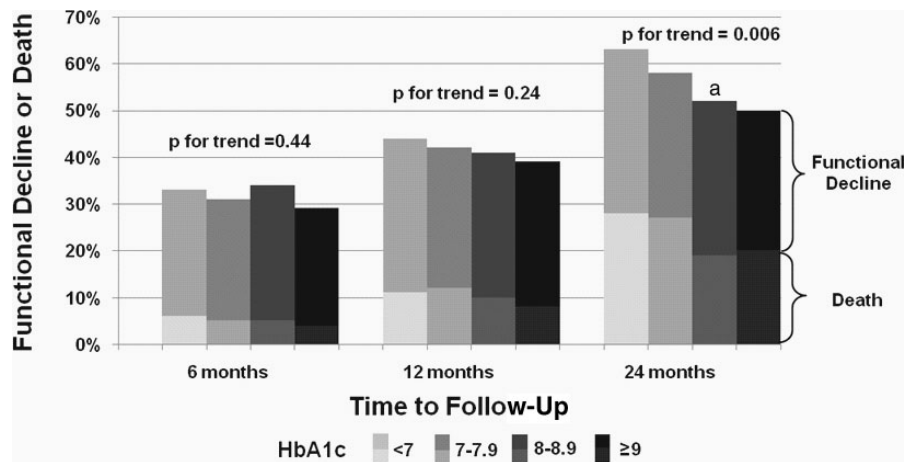
**Table 1. Participant Characteristics (N = 367)**

Characteristic	Value
Glycosylated hemoglobin measurements, n	1,579
Age, mean $\pm$ standard deviation	80 $\pm$ 9
Female, n (%)	246 (67)
Race or ethnicity, n (%)	
White	54 (15)
African American	32 (9)
Hispanic	42 (12)
Asian	239 (65)
Months enrolled in On-Lok, median (range)	18 (6–53)
Medications, n (%)	
No antihyperglycemic medications	66 (18)
Oral antihyperglycemic medications (no insulin)	116 (32)
Insulin	185 (50)
Baseline activity of daily living score, n (%)	
10–9	124 (34)
8–7	83 (23)
6–5	92 (25)
$\leq 4$	68 (19)
Hospitalizations or emergency department visits, n (%)	
None	176 (48)
Only emergency department visits	38 (10)
Hospitalizations	153 (42)
Short Portable Mental Status Questionnaire score, n (%)	
7–10	78 (21)
$\leq 6$	289 (79)
Comorbidities, n (%)	
Chronic obstructive pulmonary disease	70 (20)
Congestive heart failure	125 (34)
Cancer	27 (7)
Kidney disease	42 (11)
End-stage renal disease	17 (5)

occurred after 25% of HbA1c measurements, and the combined outcome of functional decline or death occurred after 58% of HbA1c measurements (Table 2). Participants who experienced functional decline before death were considered to have experienced the functional decline outcome and the death outcome. Because these participants are only counted once for the combined outcome of functional decline or death, the combined outcome is less than the sum of the individual outcomes.

There was evidence of treatment intensification in response to poor glycemic control, with decreases in HbA1c when initial HbA1c levels were 8.0% to 8.9% and 9.0% or greater. Conversely, there was evidence of appropriate less-aggressive treatment in participants with a baseline HbA1c level less than 7.0%. There was no change in the level of glycemic control in the reference group, with mean HbA1c staying at 7.4%.

In the fully adjusted analysis, HbA1c levels of 8.0% to 8.9% were associated with the best outcomes, with the lowest relative risk (RR) of death, functional decline, and the combined outcome of functional decline or death (Table 2). For the combined outcome, HbA1c of 8.0% to 8.9% was associated with a statistically significantly lower RR (0.88, 95% confidence interval (CI) = 0.79–0.99) compared with the reference group of HbA1c 7.0% to 7.9%. Across all outcomes (death, functional decline, and combined outcome), participants with a HbA1c level less than 7.0% had the highest risk of poor outcomes.



**Figure 1.** Functional decline or death over time according to glycosylated hemoglobin (HbA1c) level. <sup>a</sup> $P = .03$  for difference between reference group (HbA1c 7.0–7.9%) and HbA1c 8.0–8.9%. All other comparisons with reference group (HbA1c 7.0–7.9%),  $P > .05$ .

### Results Stratified According to Use of Oral Antihyperglycemic Medications and Insulin

The analysis stratified according to medications showed qualitatively similar results for the oral antihyperglycemic medications and insulin subgroups. Both groups showed a U-shaped relationship between HbA1c and the outcomes. In the oral antihyperglycemic and insulin groups, HbA1c level of 8.0% to 8.9% conferred the lowest adjusted RR of the combined outcome of functional decline or death (Table 3). This result reached statistical significance in the insulin group (RR = 0.82, 95% CI = 0.71–0.96) but not the oral antihyperglycemic group (RR = 0.89, 95% CI = 0.72–1.10). Although the results were qualitatively similar between the insulin and oral antihyperglycemic medication subgroups, there was evidence of statistical interaction across medication strata ( $P = .04$ ).

### DISCUSSION

Contrary to the original hypothesis, HbA1c above the AGS guideline-recommended target of 8.0% is not associated with a higher risk of functional decline or mortality for community-dwelling, NH-eligible elderly adults with diabetes mellitus. HbA1c of 8.0% to 8.9% was associated with a lower risk of 2-year functional decline or death than HbA1c 7.0% to 7.9%.

These results suggest that the 2003 AGS guideline recommending a HbA1c target of 8.0% or lower may need to be revisited and possibly updated.<sup>16</sup>

Glycemic control is a core element of diabetes mellitus care, and HbA1c has become the cornerstone measure of the quality of diabetes mellitus care.<sup>22,23</sup> Much of the research on optimal levels of glycemic control has focused on younger individuals, and there are few studies on the appropriate levels of glycemic control in NH-eligible elderly adults, who make up a large and growing segment of the population with diabetes mellitus. Although guidelines agree that glycemic control should be less aggressive for elderly adults with advanced illness and limited life expectancy, there is substantial disagreement over what

the specific target should be. Besides the AGS guidelines which recommend HbA1c of 8.0% or less, the Department of Veterans Affairs and Department of Defense (VA/DoD) recommend a target HbA1c of 8.0% to 9.0%,<sup>24</sup> and the American Diabetes Association recommends a “less stringent” target than HbA1c less than 7.0% for frail elderly adults.<sup>25</sup> The current study suggests that the VA/DoD guidelines may be the most-appropriate HbA1c target for community-dwelling, NH-eligible elderly adults with diabetes mellitus.

Because the glycemic control of the group with HbA1c 8.0% to 8.9% improved during the study, one possible interpretation of the results is that treatment to improve glycemic control may have contributed to the better outcomes in this group. Specifically, the group with HbA1c of 8.0% to 8.9% had a baseline mean HbA1c of 8.5%, which dropped to 8.1% at 2-year follow-up, suggesting that treatments were intensified to improve glycemic control. Because mean HbA1c level remained above the target HbA1c of 8.0%, the results suggest that the current recommended HbA1c target of 8.0% or lower is lower than necessary to maintain function.

A second interpretation of the findings is that the reference group with HbA1c of 7.0% to 7.9% may have had many declining individuals with marginal nutritional status, leading to the group with HbA1c 8.0% to 8.9% having better outcomes. This interpretation is unlikely because the HbA1c level of the reference group did not change from baseline to 24 months (mean 7.4% at baseline and 24 months). If this group included declining participants with marginal nutritional status, a decrease in HbA1c levels would be expected over 2 years of follow-up. In addition, HbA1c of 7.0% to 7.9% was chosen as the reference group rather than the group with HbA1c of less than 7% to minimize the chances of including declining participants in the reference group. Thus, although the reference group may have had some participants whose glycemic control improved because of advancing illness, it is unlikely that this fully explains the findings.

A stratified analysis was performed to determine whether the relationship between HbA1c and function

**Table 2. Risk of Functional Decline or Death at 2 Years According to Baseline Level of Glycosylated Hemoglobin (HbA1c) (All Enrollees with Diabetes Mellitus)**

HbA1c, %	HbA1c Measurements, n	Baseline HbA1c,%	HbA1c at 24 Months,%	Died, %	Adjusted RR for Death (95% CI)	Functional Decline,%	Adjusted RR for Functional Decline (95% CI)	Functional Decline or Death, <sup>a</sup>	Adjusted RR for Functional Decline or Death (95% CI)
	Mean ± standard deviation								
<7.0	698	6.3 ± 0.03	6.5 ± 0.1	29	1.06 (0.92–1.21)	53	1.07 (0.95–1.21)	63	1.07 (0.98–1.17)
7.0–7.9	412	7.4 ± 0.02	7.4 ± 0.1	29	Reference	46	Reference	58	Reference
8.0–8.9	223	8.5 ± 0.02	8.1 ± 0.1	22	0.95 (0.80–1.13)	46	0.90 (0.78–1.05)	52	0.88 (0.79–0.99)
≥9.0	246	10.2 ± 0.2	8.9 ± 0.2	22	1.09 (0.91–1.29)	45	0.98 (0.82–1.16)	50	0.97 (0.84–1.12)

Adjusted models accounted for age, sex, race or ethnicity, time enrolled in On Lok, baseline activities of daily living, comorbidities (cancer, congestive heart failure, chronic obstructive lung disease, renal disease, dialysis), and medications (none, oral medication, insulin).

<sup>a</sup> Because many participants experienced functional decline before death, the combined category of percentage with functional decline or death is not the sum of the individual percentages of the death and functional decline categories.

RR = relative risk; CI = confidence interval.

**Table 3. Risk of Functional Decline or Death at 2 Years According to Baseline Level of Glycosylated Hemoglobin (HbA1c) (Stratified Analysis)**

HbA1c, %	HbA1c Measurements, n	Baseline HbA1c,%	HbA1c at 24 Months, %	Died, %	Adjusted RR for Death (95% CI)	Functional Decline,%	Adjusted RR for Functional Decline (95% CI)	Functional Decline or Death, % <sup>a</sup>	Adjusted RR for Functional Decline or Death (95% CI)
	Mean±Standard Deviation								
Oral antihyperglycemic medications									
<7.0	241	6.3 ± 0.1	6.5 ± 0.1	25	0.97 (0.71–1.33)	61	1.17 (0.95–1.44)	67	1.18 (0.99–1.40)
7.0–7.9	159	7.4 ± 0.02	7.3 ± 0.1	19	Ref	42	Ref	48	Ref
8.0–8.9	54	8.5 ± 0.04	7.9 ± 0.2	20	1.16 (0.76–1.77)	42	0.88 (0.70–1.09)	48	0.89 (0.72–1.10)
≥ 9.0	45	10.0 ± 0.2	8.3 ± 0.3	20	1.16 (0.74–1.82)	36	1.10 (0.81–1.49)	42	1.09 (0.82–1.44)
Insulin									
<7.0	265	6.4 ± 0.03	6.7 ± 0.1	36	1.11 (0.94–1.30)	53	1.04 (0.90–1.21)	66	1.04 (0.92–1.17)
7.0–7.9	225	7.4 ± 0.02	7.5 ± 0.1	35	Ref	51	Ref	64	Ref
8.0–8.9	164	8.5 ± 0.03	8.2 ± 0.1	21	0.90 (0.73–1.11)	46	0.84 (0.70–1.02)	51	0.82 (0.71–0.96)
≥ 9.0	201	10.2 ± 0.2	9.0 ± 0.2	22	1.04 (0.84–1.28)	47	0.92 (0.74–1.14)	51	0.91 (0.76–1.08)

Adjusted models accounted for age, sex, race or ethnicity, time enrolled in On Lok, baseline activities of daily living, comorbidities (cancer, congestive heart failure, chronic obstructive lung disease, renal disease, dialysis), and medications (none, oral medication, insulin).

<sup>a</sup> Because many participants experienced functional decline before death, the combined category of percentage with functional decline or death is not the sum of the individual percentages of the death and functional decline categories.

RR = relative risk; CI = confidence interval.

differed between participants taking insulin and those taking oral medications. Overall, the stratified analysis showed that the results were similar in participants taking insulin and oral medications. In the insulin and oral medication groups, the best outcomes occurred in participants with HbA1c of 8.0% to 8.9%. In both groups, HbA1c greater than 9.0% appeared to be associated with worse outcomes than HbA1c of 8.0% to 8.9%, suggesting that HbA1c of 9% or higher should be avoided. Finally, HbA1c less than 7.0% was associated with the worst outcomes, suggesting that this is a high-risk group for functional decline that may require additional support to maintain function.

The results of the unadjusted interval analysis show that there was no significant association between HbA1c and functional decline or death at 6 months, although a trend appears to start to develop at 12 months, with higher HbA1c being associated with lower rates of functional decline or death ( $P = .24$ ). At 2 years, this result becomes statistically significant ( $P = .006$ ), suggesting that the functional benefits of HbA1c of 8.0% to 8.9% take 1 to 2 years to realize. In contrast, previous studies in younger participants suggest that approximately 8 years of tight glycemic control (HbA1c 7.0%) is needed to see lower rates of microvascular complications.<sup>16</sup> Thus, the current study suggests that, for maintaining function in community-dwelling, NH-eligible elderly adults, the HbA1c target can be between 8.0% and 8.9% and the benefits are seen within 2 years.

### Strengths, Limitations, and Next Steps

The study has strengths and limitations. The major strength was that it is the first published study to examine the longitudinal relationship between glycemic control and functional outcomes in PACE enrollees with diabetes mellitus. Much of what is known about frail elderly adults is based on NH populations, even though more elderly adults who are eligible for NH care live in the community.<sup>2</sup> Thus, this is the first study to examine the relationship between glycemic control and functional outcomes in community-dwelling, NH-eligible elderly adults.

The study may also inform the care of healthier elderly adults who are not NH eligible. Previous intervention trials of glycemic control have focused on younger, healthier individuals, whereas the current study focused on NH-eligible older adults in poorer health. Thus, the current study and previous trials represent “bookends,” highlighting the levels of glycemic control associated with best outcomes across the spectrum of health in older adults. By focusing on NH-eligible elderly adults in poorer health, this study provides important additional data to clinicians, allowing them to rationally individualize glycemic targets for individuals who are healthy, in poor health, or somewhere in between.

This study needs to be interpreted in light of its limitations. First, it was observational, and On Lok clinicians may have treated individual study participants more or less aggressively for a variety of unmeasured reasons. This confounding by indication suggests that study participants who had HbA1c levels of 7.0% to 7.9% are probably different from study participants who had lower or higher

HbA1c levels. Attempts to account for these differences were made by adjusting for demographic factors, comorbidities, and baseline function and by stratifying according to glycemic treatment (oral antihyperglycemic medications vs insulin), but it was not possible to account for other possibly important factors such as social support, which may affect glycemic control and functional decline.<sup>26</sup> Thus, some residual confounding is likely, suggesting that the results are a basis for future studies rather than a definitive statement of the optimal levels of glycemic control for community-dwelling, NH-eligible elderly adults with diabetes mellitus.

Second, although HbA1c has been shown to correlate tightly with glucose levels in most individuals, other factors, including race and red blood cell (RBC) turnover, can lead to HbA1c levels that are less indicative of glycemic control. For example, individuals treated with iron or erythropoietin therapy may have greater RBC turnover, leading to lower HbA1c levels, which may have contributed to the worse outcomes observed for participants with low HbA1c.<sup>27</sup> Nevertheless, regardless of the shortcomings of the HbA1c test, it is the most widely used test of glycemic control, and this study suggests that HbA1c levels less than 7.0% are predictive of worse outcomes.

Third, individuals and families must choose to enroll in PACE programs, and elderly adults who choose to enroll are probably different from those who do not. Next, the participants were predominantly Asian because of the history and location of On Lok in San Francisco, and there may be ethnic differences in the relationship between glycemic control and outcomes.<sup>28–30</sup> Finally, this study design cannot address the mechanisms underlying the observed associations between levels of glycemic control and outcomes.

Further research is needed. First, the observational results suggest that a HbA1c goal of 8.0% to 8.9% may be reasonable in community-dwelling, NH-eligible individuals. Because of concerns about residual confounding, a randomized trial is required to confirm or refute this observational result. Second, this study highlights the importance of nonvascular outcomes in geriatric diabetes mellitus research.<sup>31</sup> Future research should focus on outcomes such as incontinence, falls, and quality of life, along with mortality, stroke, and myocardial infarction.

In summary, in community-dwelling, NH-eligible individuals with diabetes mellitus, HbA1c levels between 8.0% and 8.9% appear to be associated with less functional decline or death at 2 years than HbA1c levels between 7.0% and 7.9%, suggesting that the current AGS HbA1c target of 8.0% or less for frail elderly adults may be lower than necessary to maintain function and delay death for this vulnerable population.

### ACKNOWLEDGMENTS

Presented as an oral plenary abstract at the Society of General Internal Medicine Annual National Meeting in Phoenix, Arizona, May 7, 2011, and as an oral abstract at the Bay Area Clinical Research Symposium in San Francisco, California, November 4, 2011.

**Conflict of Interest:** The editor in chief has reviewed the conflict of interest checklist provided by the authors

and has determined that the authors have no financial or any other kind of personal conflicts with this paper. Dr. Lee's effort was supported by National Institutes of Health, National Center for Research Resources, OD, University of California at San Francisco, Clinical and Translational Science Institute Grant KL2 RR024130 and the Hellman Family Award for Early Career Faculty at University of California at San Francisco.

**Author Contributions:** Dr. Yau designed the study, interpreted the data, and wrote the manuscript. Dr. Eng and Ms. Rice-Trumble supported data collection and provided critical revisions of the manuscript. Ms. Cenzer provided statistical support and provided critical revisions of the manuscript. Dr. Boscardin supervised the statistical analysis and provided critical revisions of the manuscript. Dr. Lee provided supervision in all phases of the study. No other parties contributed substantially to this research or to preparation of this manuscript.

**Sponsor's Role:** The funding sources had no role in the design or conduct of the study, data management or analysis, or manuscript preparation

## REFERENCES

1. Resnick HE, Heineman J, Stone R et al. Diabetes in U.S. nursing homes, 2004. *Diabetes Care* 2008;31:287–288.
2. Manton KG, Corder LS, Stallard E. Estimates of change in chronic disability and institutional incidence and prevalence rates in the U.S. elderly population from the 1982, 1984, and 1989 National Long Term Care Survey. *J Gerontol* 1993;48:S153–S166.
3. Gregg EW, Beckles GL, Williamson DF et al. Diabetes and physical disability among older U.S. adults. *Diabetes Care* 2000;23:1272–1277.
4. Gregg EW, Mangione CM, Cauley JA et al. Diabetes and incidence of functional disability in older women. *Diabetes Care* 2002;25:61–67.
5. Sinclair AJ, Allard I, Bayer A. Observations of diabetes care in long-term institutional settings with measures of cognitive function and dependency. *Diabetes Care* 1997;20:778–784.
6. Giles LC, Hawthorne G, Crotty M. Health-related quality of life among hospitalized older people awaiting residential aged care. *Health Qual Life Outcomes* 2009;7:71.
7. Schroll M, Schlettwein D, van Staveren W et al. Health related quality of life and physical performance. SENECA 1999. *J Nutr Health Aging* 2002;6:15–19.
8. Guralnik JM, Fried LP, Salive ME. Disability as a public health outcome in the aging population. *Annu Rev Public Health* 1996;17:25–46.
9. Keeler E, Guralnik JM, Tian H et al. The impact of functional status on life expectancy in older persons. *J Gerontol A Biol Sci Med Sci* 2010;65A:727–733.
10. Araki A, Ito H. Diabetes mellitus and geriatric syndromes. *Geriatr Gerontol Int* 2009;9:105–114.
11. Chen LK, Chen YM, Lin MH et al. Care of elderly patients with diabetes mellitus: A focus on frailty. *Ageing Res Rev* 2010;9(Suppl 1):S18–S22.
12. Chen LK, Lin MH, Lai HY et al. Care of patients with diabetes mellitus in long-term care facilities in Taiwan: diagnosis, glycemic control, hypoglycemia, and functional status. *J Am Geriatr Soc* 2008;56:1975–1976.
13. Nelson JM, Dufraux K, Cook PF. The relationship between glycemic control and falls in older adults. *J Am Geriatr Soc* 2007;55:2041–2044.
14. Schwartz AV, Vittinghoff E, Sellmeyer DE et al. Diabetes-related complications, glycemic control, and falls in older adults. *Diabetes Care* 2008;31:391–396.
15. Shorr RI, Ray WA, Daugherty JR et al. Incidence and risk factors for serious hypoglycemia in older persons using insulin or sulfonylureas. *Arch Intern Med* 1997;157:1681–1686.
16. Brown AF, Mangione CM, Saliba D et al. Guidelines for improving the care of the older person with diabetes mellitus. *J Am Geriatr Soc* 2003;51(Suppl Guidelines):S265–S280.
17. Bodenheimer T. Long-term care for frail elderly people—the On Lok model. *N Engl J Med* 1999;341:1324–1328.
18. Eng C, Pedulla J, Eleazer GP et al. Program of All-inclusive Care for the Elderly (PACE): An innovative model of integrated geriatric care and financing. *J Am Geriatr Soc* 1997;45:223–232.
19. Vijan S, Hofer TP, Hayward RA. Estimated benefits of glycemic control in microvascular complications in type 2 diabetes. *Ann Intern Med* 1997;127:788–795.
20. Caruso LB, Silliman RA, Demissie S et al. What can we do to improve physical function in older persons with type 2 diabetes? *J Gerontol A Biol Sci Med Sci* 2000;55A:M372–M377.
21. Lee SJ, Boscardin WJ, Stijacic Cenzer I et al. The risks and benefits of implementing glycemic control guidelines in frail older adults with diabetes mellitus. *J Am Geriatr Soc* 2011;59:666–672.
22. Standards of medical care for patients with diabetes mellitus. American Diabetes Association *Diabetes Care* 2002;25:213–229.
23. Ahmann AJ. Guidelines and performance measures for diabetes. *Am J Manag Care* 2007;13(Suppl 2):S41–S46.
24. Pogach LM, Brietzke SA, Cowan CL, Jr et al. Development of evidence-based clinical practice guidelines for diabetes: The Department of Veterans Affairs/Department of Defense guidelines initiative. *Diabetes Care* 2004;27(Suppl 2):B82–B89.
25. Standards of medical care in diabetes—2007. American Diabetes Association *Diabetes Care* 2007;30(Suppl 1):S4–S41.
26. Okura T, Heisler M, Langa KM. Association between cognitive function and social support with glycemic control in adults with diabetes mellitus. *J Am Geriatr Soc* 2009;57:18160–18240.
27. Ng JM, Cooke M, Bhandari S et al. The effect of iron and erythropoietin treatment on the A1C of patients with diabetes and chronic kidney disease. *Diabetes Care* 2010;33:2310–2313.
28. Bryson CL, Ross HJ, Boyko EJ et al. Racial and ethnic variations in albuminuria in the US Third National Health and Nutrition Examination Survey (NHANES III) population: associations with diabetes and level of CKD. *Am J Kidney Dis* 2006;48:720–726.
29. Kehl KG, Findeisen HM, Fardo DW et al. Race-ethnicity as an effect modifier of the association between HbA1c and mortality in U.S. adults without diagnosed diabetes. *Eur J Endocrinol* 2011;165:275–281.
30. McWilliams JM, Meara E, Zaslavsky AM et al. Differences in control of cardiovascular disease and diabetes by race, ethnicity, and education: U.S. trends from 1999 to 2006 and effects of Medicare coverage. *Ann Intern Med* 2009;150:505–515.
31. Lee SJ, Eng C. Goals of glycemic control in frail older patients with diabetes. *JAMA* 2011;305:1350–1351.