Better Glycemic Control Is Associated With Maintenance of Lower-Extremity Function Over Time in Mexican American and European American Older Adults With Diabetes

CHEN-PIN WANG, PHD[1]
HELEN P. HAZUDA, PHD[2,3]

OBJECTIVE—Diabetes is a major cause of functional decline among older adults, but the role of glycemic control remains unclear. This article assesses whether better glycemic control is associated with better maintenance of lower-extremity function over time in older adults with diabetes.

RESEARCH DESIGN AND METHODS—Participants (n = 119) in the San Antonio Longitudinal Study of Aging, ages 71–85, who met American Diabetes Association diabetes criteria were followed over a 36-month period. Seven measures of A1C (HbA_{1c}) were obtained at 6-month intervals; three measures of lower-extremity function were obtained at 18-month intervals using the Short Physical Performance Battery (SPPB). A two-step analytic approach was used, first, to identify distinct glycemic control classes using latent growth mixture modeling and, second, to examine trajectories of lower-extremity function based on these classes using path analysis.

RESULTS—Two glycemic control classes were identified: a poorer control class with higher means (all >7%) and higher within-subject variability in HbA_{1c} and a better control class with lower means (all <7%) and lower within-subject variability. The short-term and long-term maintenance of lower-extremity function, assessed by the association between the first and second SPPB measures and the first and third SPPB measures, were both greater in the better control class than in the poorer control class.

CONCLUSIONS—Among older adults with diabetes, better glycemic control may improve both short-term and long-term maintenance of lower-extremity function.

Diabetes Care 34:268–273, 2011

Diabetes is a major public health problem in U.S. older adults, with prevalence of diagnosed and undiagnosed diabetes exceeding 17% in both sexes (1). Moreover, it has been estimated that approximately 25% of older adults (>1.2 million) with diabetes are unable to walk one-fourth mile, climb 10 stairs, or do housework and approximately 50% (>2.5 million) have difficulty performing these tasks (2). Among women, yearly incidence of any functional disability among those with diabetes has been estimated at 9.8% compared with an incidence of 4.8% among those without diabetes (3). Among older Mexican Americans of both sexes, the rate of decline in functional status has been reported to be more rapid among those with diabetes versus those without diabetes (4). Cross-sectional analyses from the Health, Aging, and Body Composition Study (Health ABC) suggested that A1C (HbA_{1c} < vs. ≥ 7%) may explain the association of diabetes with subclinical functional limitation (5). In addition, longitudinal analyses of the association of diabetes with mobility- and activity of daily living (ADL) disability in a subsample of participants in the Women's Health and Aging Study (WHAS) suggested that adjustment for HbA_{1c} reduces the excess diabetes-associated risk of such disability by 36–65% (6). However, no longitudinal analyses have examined the role of glycemic control in physical functional decline in both sexes or in cohorts that include large proportions of Mexican Americans as well as European Americans.

The current study uses longitudinal data from the San Antonio Longitudinal Study of Aging (SALSA), a community-based study of disablement in a biethnic cohort of Mexican Americans and European Americans to examine whether better glycemic control improves the maintenance of lower-extremity physical function over a 36-month period among participants with diabetes.

RESEARCH DESIGN AND METHODS

Sample

Subjects were participants in the SALSA, a community-based study of the disablement process in Mexican American (MA) and European American (EA) older adults, composed of a baseline examination (1992–1996) and follow-up study (2000–2005), an average of 6.9 years later. The oldest members (age 65+ years) of the San Antonio Heart Study (SAHS) cohort, a community-based study of ethnic differences in risk factors for diabetes and cardiovascular disease, were recruited to participate in the SALSA baseline study.

From the [1]Department of Epidemiology and Biostatistics, University of Texas Health Science Center at San Antonio, San Antonio, Texas; the [2]Supervisory Research Health Scientist, Research Service, Department of Veterans Affairs, Audie Murphy Medical Center, San Antonio, Texas; and the [3]Department of Medicine, University of Texas Health Science Center at San Antonio, San Antonio, Texas.
Corresponding author: Helen P. Hazuda, hazuda@uthscsa.edu.
Received 21 July 2010 and accepted 22 October 2010.
DOI: 10.2337/dc10-1405
The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States government.

In the SAHS, subjects were randomly sampled from low-, middle-, and high-income neighborhoods in order to provide a cohort with comparable numbers of MAs and EAs and to maximize sociocultural variation among MAs in the study; details of the SAHS study design, sampling approach, recruitment, and field procedures have been described previously (7). The SALSA baseline response rate was 70.5% (749 of 1,062 eligible candidates); there was no evidence of major response bias to the SAHS survey among people who later became SALSA age-eligible and no evidence of major attrition bias between the initial SAHS survey and the SALSA survey.

The SALSA follow-up study included three visits 18 months apart for all participants. Among those diagnosed with diabetes, HbA_{1c} was also assessed at 6-month intervals. The response rates among baseline survivors were: follow-up 1, 79.1% (474 of 599); follow-up 2, 73.4% (413 of 563); and follow-up 3, 71.0% (375 of 528). There was no evidence of major response bias over the follow-up interval. The sample for the current study is the subset of 119 subjects who participated in the follow-up study and had diagnosed diabetes at the time that study began.

The SALSA baseline and follow-up studies were approved by the Institutional Review Board of the University of Texas Health Science Center at San Antonio, and all subjects gave informed consent.

Measures

Assessments were conducted by trained, bilingual staff using standardized protocols. Diabetes was classified based on American Diabetes Association criteria (8) as a fasting plasma glucose ≥126 mg/dL or current diabetic medication use. Lower-extremity physical functional limitation was measured with the Short Physical Performance Battery (SPPB), a well-established, validated measure constructed from 8-foot walking time, repeated chair stands, and balance scores (9). Higher scores indicate better performance and less functional limitation. Angina was assessed with the Rose questionnaire (10); stroke was assessed as self-reported doctor-diagnosed disease. Hypertension was assessed using guidelines in the sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (11) as a systolic pressure ≥140 mmHg or a diastolic pressure ≥90 mmHg or current antihypertensive medication. Pulmonary function was assessed as forced expiratory volume at 1 s (FEV_1) measured with the Welch-Allyn Pneumocheck (Skaneateles, NY) (12). BMI was measured as weight in kilograms divided by height in meters squared. Ethnic background was classified using a standardized, validated algorithm (13). Education (years of formal schooling) was ascertained by self-report.

Ankle-brachial pressure indexes (ABIs) were calculated as the ratio of the higher systolic pressure of the dorsalis pedis or posterior tibial for each leg over the mean of the right and left brachial systolic blood pressure. Peripheral arterial disease (PAD) was defined as an ABI <0.9 in either leg and was considered absent if an ABI of 0.9–1.3 was present in both legs. An ABI >1.3 was defined as high and noncompressible. Based on evidence suggesting equivalence of low and high ABIs (14), the latter were considered as having PAD.

Peripheral nerve dysfunction (PND) was measured as vibration perception threshold (VPT) (15) using a Horwell Neurothesiometer with the probe balanced vertically on the pulp of the great toe. The neurothesiometer measures sensitivity in detecting sensory vibratory stimuli. Scores (0–50) were the mean of three readings with scores for the right foot used in the analyses. Higher scores indicate worse PND.

Analysis

We used a two-step analytic approach, which incorporated the latent growth mixture modeling (LGMM) technique into a path analysis. The first step was to use LGMM (16) to identify statistically distinct glycemic control classes and to quantify subjects' glycemic control status based on seven repeated measures of HbA_{1c}. A subject's glycemic control status was assessed by the likelihood of being in each glycemic control class or, specifically, by the propensity score (or posterior probability) of being in each class given the subject's observed HbA_{1c} measures, covariates, and the LGMM analysis result. In the second step, these propensity scores were incorporated as weights (reflecting the probability of being in each glycemic control class) in the path modeling of SPPB scores to assess the class-specific relationship among SPPB scores.

To elaborate further, LGMM was used in step 1 to quantify subjects' glycemic control status (or class) since it is an exploratory multivariate statistical technique, analogous to cluster analysis for longitudinal data, which permits the identification of distinct latent classes in a study while adjusting for covariates. For the current study, the unobserved latent classes were determined based on the similarity of the patterns of the seven repeated measures of HbA_{1c} collected over a 36-month period at 6-month intervals. The patterns of HbA_{1c} measures were based on both the means and the within-subject variability of these measures over time. LGMM analyses require specification of the number of latent classes and the pattern of repeated measures for each class. Covariates included in the LGMM analysis were age, sex, ethnicity, education, BMI, and hypertension. To determine the best fit LGMM to the data, we used two goodness-of-fit indexes, Akaike information criterion, and Bayesian information criterion, as well as residual diagnostics (17). Each subject's glycemic control class (HbA_{1c} trajectories) identified by LGMM analyses was characterized in terms of the subject's propensity score (or the likelihood) for membership in each glycemic control class. For example, in a model with two latent classes, propensity scores of 0.9 and 0.1 for a given subject suggest that he or she is likely to belong to the first class with a probability of 0.9 (90%) and to the second class with a probability of 0.1 (10%). In step 2, these propensity scores were then used as weights in path analyses of SPPB scores during the three follow-ups. More specifically, this mixture path modeling was used to assess the class-specific effect of lower-extremity functioning (measured by SPPB) in follow-up 1 on functioning in follow-ups 2 and 3 while adjusting for covariate effects and the class-specific effect of SPPB in follow-up 2 on functioning in follow-up 3. Covariates included in the path analyses were age, education, ethnicity, BMI, angina, stroke, and pulmonary function (FEV_1) measured at follow-up 1.

The research question (whether the impact of baseline functional status on subsequent functioning over 18- and 36-month periods can be improved by better glycemic control) was addressed by comparing the adjusted correlations between SPPB at follow-up 1 and at follow-up 2 as well as between SPPB at follow-up 1 and at follow-up 3 across the identified glycemic control classes. Mplus software (18) was used to obtain model estimates. In the step 1 analysis, subjects with missing data on the covariates or all HbA_{1c} values (N = 2) were excluded from the analyses; in step 2, subjects with missing values on the covariates (N = 6) or all SPPB values (N = 4) were excluded. The total number of subjects included in the step 2 analysis

was 107. Partial missing data on HbA_{1c} and SPPB were addressed utilizing the full-information maximum likelihood (FIML) method. FIML uses the entire set of the observed data matrix to estimate parameters. In contrast with list-wise deletion or multiple imputations, FIML yields unbiased parameter estimates when data are missing at random and preserves the overall power and efficiency of the analysis (17).

To further characterize the latent classes identified in step 1, a pseudoclass estimation technique (17) was used to calculate for each glycemic control class *1*) the proportion of subjects who were newly diagnosed with diabetes, *2*) the proportion of subjects who had PAD, and *3*) the means and standard deviations of VPT and diabetes duration.

RESULTS—Sample characteristics are described in Table 1. As shown in Fig. 1, two latent classes of HbA_{1c} trajectories were identified: one with higher means and greater within-subject variability in HbA_{1c} over time (called the poorer glycemic control class, 55.3% of the sample) and the other class (called the better glycemic control class, 44.7% of the sample) with lower means and less within-subject variability in HbA_{1c} over time. These two classes are statistically distinct as well as clinically meaningful because the means of the seven repeated measures of HbA_{1c} in the poorer control class were all greater than 7%, whereas the corresponding means in the better control class were all below 7%, the clinical threshold commonly used to designate acceptable glycemic control. Membership in the better control class versus the poorer control class was associated with older age and higher education level (the odds ratios for 1 additional year of age and education were 6.88 and 1.13, respectively). Although the proportion of those newly diagnosed with diabetes in the better glycemic control class compared with the poorer control class was 30.4% vs. 17.1%, average years of diabetes duration in the better control class was only slightly less than that in the poorer control class (11.4 ± 11.5 vs. 12.8 ± 11.5). Although the proportion of subjects with PAD was lower in the better control class than in the poorer control class (47.8% vs. 51.7%), the average VPT was somewhat higher (19.4 ± 11.8 vs. 17.8 ± 10.6, respectively).

The associations of SPPB at follow-up 1 with SPPB at follow-ups 2 and 3 are shown in Table 2. The covariate-adjusted association between SPPB scores measured at follow-ups 1 and 2 was greater in the better control class than that in the poorer control class (adjusted correlation 0.86 and 0.68, respectively), suggesting that the short-term impact of baseline SPPB on SPPB scores 18 months after baseline was also greater in the better glycemic control class than that in the poorer control class. In addition, the magnitude of the positive association between SPPB at follow-up 1 and follow-up 3, adjusted for baseline covariates and SPPB at

Table 1—*Sample characteristics*

Variable*	%	Mean (SD)	Range
Age (years)		76.3 (3.4)	7–85
Female (%)	54.6		
Mexican American (%)	71.4		
Education (years)		10.2 (4.9)	0–20
Household income (category)		12.8 (4.0)	2–19
Diabetes duration (years)		12.5 (11.2)	0–51
Newly diagnosed for diabetes	22.7		
PVD	50.4		
VPT		18.5 (11.2)	0–50
BMI (kg/m^2)		29.7 (5.2)	18.4–47.7
Forced expiratory volume at 1 s (liters)		1.6 (0.6)	0.4–3.7
Angina (%)	15.4		
Stroke (%)	18.6		
Hypertension (%)	73.1		
SPPB		7.6 (3.4)	0–12
Walking times		2.8 (1.2)	0–4
Balance		2.5 (1.4)	0–4
Chair stands		2.0 (1.3)	0–4

*A household income category of 12.8 equals ~$23,800 annually; angina and stroke were assessed by self-report; presence of hypertension was assessed as a systolic pressure ≥140 mmHg or a diastolic pressure ≥90 or current antihypertensive medication.

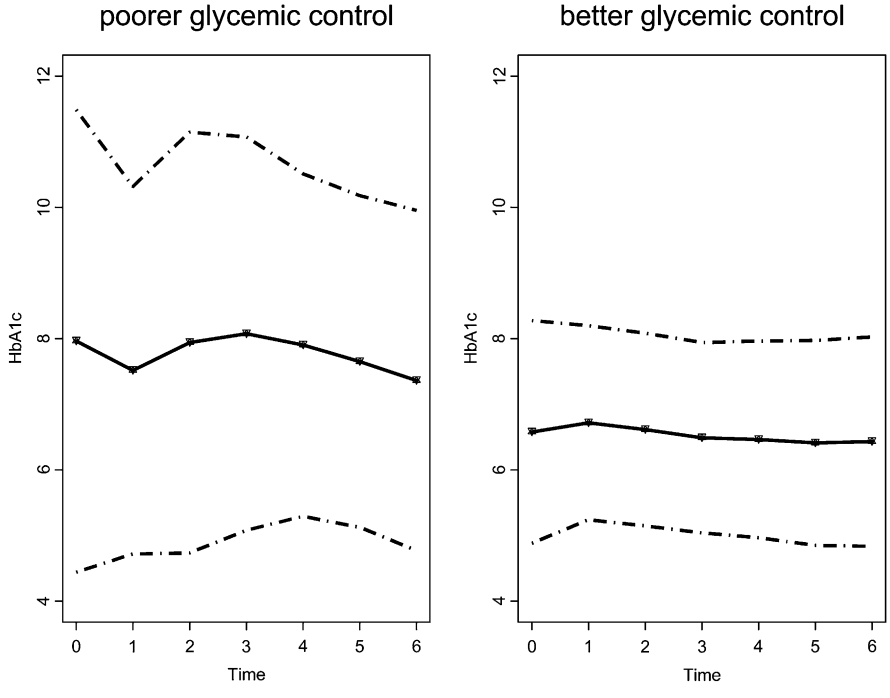

Figure 1—*Mean trajectories of two latent classes estimated by LGMM of HbA_{1c}. Solid line connects the means of HbA_{1c}; broken lines connect the 95% confidence bounds of the HbA_{1c} means.*

Table 2—*Covariate-adjusted correlation among SPPB scores by latent glycemic control class*

	Better glycemic control (44.7%)			Poorer glycemic control (55.3%)		
	Estimate	SE	*Z* value	Estimate	SE	*Z* value
Total SPPB						
Follow-up 1→follow-up 2	0.86	0.2	5.54**	0.68	0.1	5.09**
Follow-up 1→follow-up 3	0.62	0.2	3.74*	0.42	0.2	2.32*
Walking time						
Follow-up 1→follow-up 2	0.94	0.2	4.85**	0.50	0.2	2.84**
Follow-up 1→follow-up 3	0.87	0.2	4.43**	0.50	0.2	2.75**
Balance						
Follow-up 1→follow-up 2	0.52	0.2	3.23**	0.37	0.1	2.54*
Follow-up 1→follow-up 3	0.28	0.2	1.34	0.17	0.2	1.01
Chair stands						
Follow-up 1→follow-up 2	0.64	0.1	6.84**	0.45	0.2	2.85**
Follow-up 1→follow-up 3	0.39	0.2	2.02*	0.49	0.1	4.3**

*For effects with $0.01 \leq P$ values < 0.05. **For effects with P values < 0.01.

follow-up 2, was greater in the better glycemic control class compared with that in the poorer control class, suggesting that the long-term impact of baseline SPPB on SPPB scores 36 months later was greater in the better glycemic control class compared with the poorer control class (adjusted correlation 0.62 and 0.42, respectively). The differential temporal associations (follow-up 1 to follow-up 2 and follow-up 1 to follow-up 3) in the total SPPB score between glycemic control classes held true for the SPPB component scores with the exception of chair stands at 36 months.

CONCLUSIONS—Using a two-step analysis of 119 individuals with diabetes in the SALSA, we identified two distinct glycemic control trajectory classes based on seven repeated measures of HbA_{1c} 6 months apart: a poorer control class with higher means (all >7%) and greater within-subject variability in HbA_{1c} and a better control class with lower means (all <7%) and lower within-subject variability. At study initiation, the mean SPPB score in the better glycemic control class was 8.3 compared with 7.1 in the poorer glycemic control class, indicating that those with better glycemic control at study initiation had a meaningful, substantially better level of lower-extremity function than did those with poorer glycemic control (19). We showed that both short-term (18 month) and long-term (36 month) maintenance of lower-extremity function (measured by the SPPB) were greater in the better glycemic control class than in the poorer glycemic control class. Maintenance of lower-extremity function as assessed by the SPPB is particularly important because poor performance on this measure has been associated with increased incident disability, nursing home placement, and mortality (9).

Prior studies that examined the relationship between HbA_{1c} and physical function among older adults with diabetes (5,6) suggested that the relationship between diabetes and functional decline may be mediated by glycemic control. These studies, however, had several limitations. The Health ABC study included only well-functioning individuals in a restricted age range (70–79 years old) and examined this association cross-sectionally (5). Although the WHAS examined longitudinally whether the association of diabetes with onset of mobility- and ADL disability was mediated by HbA_{1c}, the study sample included only women who were ≥65 years old and were among the 33% most disabled women living in the Baltimore community (6). Neither study included Hispanics. The Sacramento Area Latino Study on Aging (4) reported lower baseline functional status and more rapid functional decline among older Mexican Americans with diabetes compared with those without diabetes, but data on HbA_{1c} levels were not collected. None of these prior studies examined the potential moderating effect of glycemic control on functional decline in the presence of diabetes. Our study extends these previous investigations by examining the potential moderating effect of glycemic control over time on the association between diabetes and functional decline in a cohort comprising both sex groups and large proportions of Mexican Americans as well as European Americans. Our results suggest that the level of glycemic control over time moderates both short-term and long-term maintenance of physical function in older adults with diabetes. More specifically, we found that the impact of initial SPPB scores on SPPB scores 18 and 36 months later was greater in those with better glycemic control compared with those with poor glycemic control, suggesting that the maintenance of physical function over time is improved by better glycemic control.

The mechanism by which better glycemic control improves or sustains physical function over time among people with diabetes is not yet clear. One potential mechanism, however, is by reducing or delaying the development of diabetes complications such as PAD and PND. This posited mechanism is consistent with the results of several significant prior studies. The UKPDS long-term randomized controlled trial in type 2 diabetes demonstrated that better glycemic control resulted in reduced risk of both macrovascular and microvascular complications (20). Furthermore, the association of PAD and nerve conduction velocity with lower-extremity function has been documented in a population-based study of older adults (21). With regard to the maintenance of physical function, a potential mechanism for the effect of good glycemic control may be the so-called legacy effect as shown in the UKPDS (22); that is, for patients with type 2 diabetes, if the glycemic control goal is appropriately tailored to patients' conditions at an early stage of the disease, then it could result in a long-lasting effect on the development of complications. However, the role of tailored glucose control in the disablement process (23) has received little attention in the literature.

In the current study the proportion of subjects with newly diagnosed diabetes was almost twice as high in the better glycemic control class than in the poorer control class, suggesting that shorter duration of diabetes in the former group may have been associated with a lower prevalence of complications such as PAD and PND, which, in turn, accounted for the better maintenance of lower-extremity function in this group. However, the average duration of diabetes in the better control group was only 1.4 years less than that in the poorer control group. In addition, whereas prevalence of PAD was lower in the better control group, VPT was somewhat higher. Thus our data offer a somewhat mixed picture with regard

to the potential role of differences in diabetes duration and complications between the two glycemic control classes in explaining the moderating effect of glycemic control on lower-extremity functioning.

Our study included subjects with a wide range of glycemic control over time and found a substantial association between HbA_{1c} and lower-extremity functional limitation. It may be that some studies reporting a weak or absent association of HbA_{1c} with lower-extremity complications have been conducted in cohorts composed of subjects with such long-standing, poorly controlled diabetes that the likelihood of carrying out meaningful analyses of the association of HbA_{1c} with the outcomes of interest is greatly diminished (e.g., studies of wound healing in people with diabetic foot ulcers) (24).

Based on the current findings, we hypothesize that the initial effect of an intervention designed to improve lower-extremity function in older adults with diabetes (e.g., lower-extremity strength training) will be sustained for longer periods of time in those with better glycemic control than in those with poorer control. One possible strategy for testing this hypothesis is to conduct a randomized controlled trial with the intervention and control arms balanced within clinically distinct baseline HbA_{1c} stratum (identified based on repeated measures of HbA_{1c} over a prior time period). Such a study may not only demonstrate better maintenance of physical function among subjects with better glycemic control over a 36-month period but also provide the basis for examining whether there might be an even longer benefit resulting from a legacy effect of better glycemic control. If the results of such a study were positive, they would provide evidence of an additional benefit of good glycemic control, namely, better maintenance of lower-extremity physical function. Results of the current study already suggest that, whether someone with diabetes takes part in activities specifically designed to increase the level of lower-extremity function, good glycemic control can delay or reduce subsequent functional decline.

While the current study is limited to a small number of subjects, the seven repeated measures of HbA_{1c} and three repeated measures of SPPB collected over a 36-month period provided sufficient power to demonstrate that glycemic control may moderate lower-extremity functional decline among older adults with diabetes. Generalizability of the results may be limited by the single geographic location of the study, inclusion of only Mexican American and European American participants, and the age range (71–85 years old) of the sample. Nonetheless, the study provides promising evidence to support the added benefit of good glycemic control on both short-term and long-term maintenance of physical function in the presence of diabetes.

Acknowledgments—This study was supported by National Institute on Aging (NIA) Grant 1-R01-AG10444 (SALSA), NIA Grant 1-R01-AG16518 (Disablement in an Aging, Bi-ethnic Cohort), National Institute of Diabetes and Digestive and Kidney Diseases Grant 1-K25 DK075092, and National Center for Research Resources Grant M01-RR01346 (Fredrick C. Bartter General Clinical Research Center). This material is the result of work supported with resources and the use of facilities at the Audie Murphy VA Medical Center, San Antonio, TX.

No potential conflicts of interest relevant to this article were reported.

C.P.W. wrote the article, performed data analyses, and interpreted results. H.P.H. contributed to all aspects of the article as senior author.

References

1. Harris MI, Flegal KM, Cowie CC, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988–1994. Diabetes Care 1998;21:518–524
2. Gregg EW, Beckles GL, Williamson DF, et al. Diabetes and physical disability among older U.S. adults. Diabetes Care 2000;23:1272–1277
3. Gregg EW, Mangione CM, Cauley JA, et al; Study of Osteoporotic Fractures Research Group. Diabetes and incidence of functional disability in older women. Diabetes Care 2002;25:61–67
4. Wu JH, Haan MN, Liang JL, Ghosh D, Gonzalez HM, Herman WH. Diabetes as a predictor of change in functional status among older Mexican Americans: A population-based cohort study. Diabetes Care 2003;26:314–319
5. De Rekeneire N, Resnick HE, Schwartz AV, et al; Health, Aging, and Body Composition study. Diabetes is associated with subclinical functional limitation in nondisabled older individuals: The Health, Aging, and Body Composition study. Diabetes Care 2003;26:3257–3263
6. Volpato S, Ferrucci L, Blaum C, et al. Progression of lower-extremity disability in older women with diabetes: The Women's Health and Aging Study. Diabetes Care 2003;26:70–75
7. Hazuda HP, Haffner SM, Stern MP, Eifler CW. Effects of acculturation and socioeconomic status on obesity and diabetes in Mexican Americans. The San Antonio Heart Study. Am J Epidemiol 1988;128:1289–1301
8. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 2003;26(Suppl. 1):S5–S20
9. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower-extremity function. Association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49:M85–M94
10. Rose GA, Blackburn H. *Cardiovascular Survey Methods*. Geneva, Switzerland, World Health Organization, 1968
11. National Committee on Prevention, Detection Evaluation and Treatment of High Blood Pressure. The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. Arch Intern Med 1997;157:2413–2446
12. Barkley B, Lichtenstein MJ, Garza C, Hazuda HP. Clinical validation of the Welch-Allyn Pneumocheck hand-held spirometer. Am J Med Sci 1994;308:357–359
13. Hazuda HP, Comeaux PJ, Stern MP, Haffner SM, Eifler CW, Rosenthal M. A comparison of three indicators for identifying Mexican Americans in epidemiologic research. Methodological findings from the San Antonio Heart Study. Am J Epidemiol 1986;123:96–112
14. Resnick HE, Lindsay RS, McDermott MM, et al. Relationship of high and low ankle brachial index to all-cause and cardiovascular disease mortality: the Strong Heart Study. Circulation 2004;109:733–739
15. Resnick HE, Vinik AI, Schwartz AV, et al. Independent effects of peripheral nerve dysfunction on lower-extremity physical function in old age: The Women's Health and Aging Study. Diabetes Care 2000;23:1642–1647
16. Muthen B. Beyond SEM: General latent variable modeling. Behaviormetrika 2002;29:81–117
17. Wang CP, Brown CH, Bandeen-Roche K. Residual diagnostics for growth mixture models: Examining the impact of a preventive intervention on multiple trajectories of aggressive behavior. J Am Stat Assoc 2005;100:1054–1076
18. Muthen LK, Muthen BO. *Mplus user's guide. Muthen and Muthen*. Los Angeles, CA, p. 1999–2006.
19. Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. J Am Geriatr Soc 2006;54:743–749
20. Stratton IM, Adler AI, Neil HAW, et al. Association of glycaemia with macrovascular

and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ 2000;321:405–412
21. McDermott MM, Guralnik JM, Albay M, Bandinelli S, Miniati B, Ferrucci L. Impairments of muscles and nerves associated with peripheral arterial disease and their relationship with lower extremity functioning: the InCHIANTI Study. J Am Geriatr Soc 2004;52:405–410
22. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HAW. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 2008;359:1577–1589
23. Verbrugge LM, Jette AM. The disablement process. Soc Sci Med 1994;38:1–14
24. Margolis DJ, Kantor J, Santanna J, Strom BL, Berlin JA. Risk factors for delayed healing of neuropathic diabetic foot ulcers: a pooled analysis. Arch Dermatol 2000;136:1531–1535