Inconsistent Use of Diabetes Medications, Diabetes Complications, and Mortality in Older Mexican Americans Over a 7-Year Period

Data from the Hispanic Established Population for the Epidemiologic Study of the Elderly

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OBJECTIVE — The aim of this study was to examine the relationship between inconsistency in use of diabetes drugs and risk of renal, eye, and circulation problems and death over a 7-year period in community-dwelling older Mexican Americans.

RESEARCH DESIGN AND METHODS — Data are from the four waves of the Hispanic Established Population for the Epidemiologic Study of the Elderly. In-home interviewers assessed consistency in use of diabetes medications among 908 diabetic Mexican Americans, aged ≥65 years. Diabetes and complications were by self-report. Subjects with poor consistency in use of medication were those who, at any time during the 7-year follow-up, discontinued or inconsistently used their diabetes medications and those who had no diabetic medications at home despite self-report of taking medicine for diabetes.

RESULTS — Thirty-six percent of our sample were inconsistent with diabetes medication usage. Older age and lack of supplemental health insurance were significantly associated with inconsistency of use of medication. In a multivariate logistic regression model, subjects with poor consistency in use of medication were more likely to report kidney problems (odds ratio [OR] 1.59; 95% CI 1.13–2.23; $P = 0.008$) at follow-up compared with those with good consistency, after controlling for age, sex, medication type, duration of diabetes, education, income, marital status, language of interview, insurance status, cognitive function, presence of depressive symptoms, activities of daily living, and instrumental activities of daily living. In Cox regression models, poor consistency with diabetic medication was also associated with increased all-cause mortality (hazard ratio [HR] 1.43; 95% CI 1.13–1.82; $P = 0.003$) and diabetes-related deaths (1.66; 1.20–2.30; $P = 0.002$) over a 7-year period after adjusting for relevant confounders.

CONCLUSIONS — Inconsistent use of diabetic medication was associated with an increased risk of kidney problems and deaths over a 7-year period in older Mexican Americans.

Mexican-Americans are approximately two times more likely to be diagnosed with diabetes compared with non-Hispanic Caucasians of similar age (1–7). Harris et al. (6), using the National Health and Nutrition Examination Survey (NHANES III) data, showed that prevalence of diabetes in Mexican Americans aged 40–74 years was 20.3%, whereas the rate in non-Hispanic Caucasians was 11.2%. Data from NHANES III also showed that ~33% of Mexican-American women aged 60–74 years had diabetes (defined by fasting plasma glucose >125 mg/dl or by self-report) (6).

A few studies have documented higher rates of diabetes complications (kidney, eye, and circulation problems and nontraumatic limb amputations) among diabetic Mexican Americans compared with diabetic non-Hispanic Caucasians of similar age (6,8–11). For instance data from the San Antonio Heart Study and NHANES III showed that diabetic Mexican Americans had twice the risk of diabetic retinopathy compared with diabetic non-Hispanic Caucasians (6,8). Data from the San Antonio Heart Study also showed that U.S.-born Mexican American with diabetes, aged 25–72 years, when compared with non-Hispanic Caucasians with diabetes, had greater risk of cardiovascular mortality (hazard ratio [HR] 1.66; 95% CI 1.04–2.65), whereas the risk in Mexico-born Mexican Americans was similar to non-Hispanic Caucasians (0.89; 0.40–2.01) (12). The ethnic differences in diabetes complications

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Abbreviations: ADL, activity of daily living; H-EPESE, Hispanic Established Population for the Epidemiologic Study of the Elderly; HMO, health maintenance organization; IADL, instrumental activity of daily living; MMSE, Mini Mental State Examination; NHANES III, National Health and Nutrition Examination Survey.

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

might be due to differences in diabetes biology, access to health care, health care provider practices, and patients' self-care practices including adherence to treatments (13,14).

Data from the Diabetes Control and Complications Trial research group and U.K. Prospective Diabetes Study group studies showed that adherence to diabetes medications, in addition to adequate blood pressure and lipid management, significantly lowered the risk of diabetes complications such as nephropathy, neuropathy, and retinopathy (15,16). Adherence to prescribed treatments is a critical step in achieving optimal diabetes control and good health outcome (15–18). Most of the studies on diabetic treatment have been done on predominantly non-Hispanic Caucasians and in subjects aged ≤65 years. For example, Schectman et al. (17), using data from 810 Caucasians and African-American subjects with type 2 diabetes, found that a 10% increase in diabetic drug adherence was significantly associated with a 0.16% reduction in HbA_{1c} levels. There was no information on relationship between adherence and diabetes complications in this study. Similarly, data from the Medical Outcomes Study showed a significant correlation between self-reports of diabetic treatment adherence and levels of serum glucose ($r = -0.33$) and HbA_{1c} ($r = -0.15$) (18). However, little is known about impact and predictors of inconsistency in use of diabetes medications on risk of diabetes complications in older Mexican Americans, which is one of the fastest growing ethnic groups in the U.S.

Given the high prevalence of diabetes among Mexican Americans and the need to identify potentially modifiable factors for better diabetes care, we examined the relationship between inconsistent use of diabetes drugs and risk of renal, eye, and circulation problems and death over a period of 7 years in a large probability sample of older Mexican Americans residing in five southwestern U.S. states. We hypothesized that poor consistency in use of diabetic medications (inconsistent use or discontinuation of drugs at any time in the study period) would be associated with higher risk of diabetes complications over a 7-year period, adjusting for relevant sociodemographic factors, type of diabetes medications, duration of self-reported diabetes, cognition function, presence of depressive symptoms, and daily activity levels.

RESEARCH DESIGN AND METHODS

Sample

Data are from the Hispanic Established Population for the Epidemiologic Study of the Elderly (H-EPESE). The H-EPESE is an ongoing National Institute on Aging–funded community-based study of 3,050 Mexican-American subjects aged ≥65 years (19). The sample was designed to be generalizable to ~85% of older Mexican Americans living in five Southwestern states including Texas, California, Colorado, Arizona, and New Mexico. A full description of the study, rationale, methods, and subject characteristics can be found elsewhere (19). The response rate at baseline interview (1993–1994) was 83% with 2,873 (94.2%) subjects interviewed in person and 177 (5.8%) by proxy. The sample was subsequently interviewed in 1995-1996, in 1998-1999, and in 2000-2001. Interviewers, who were fully bilingual and predominantly of Hispanic origin, conducted all interviews in Spanish or English, depending on the respondent's preference. Overall, 78.3% of all interviews were conducted in Spanish.

We used data from the four waves of H-EPESE. There were 955 subjects with self-reported diabetes over the four waves of the study: 690 subjects in the first wave, 119 in the second wave, 86 in the third wave, and 60 in the fourth wave. Diabetic subjects ($n = 29$) who were never on medications in any participated interviews and those ($n = 18$) who said "I do not know" to or refused to answer to the question "Are you taking any medicine for diabetes now?" in any follow-up interviews were excluded from the analysis. This study reports on 908 diabetic Mexican Americans aged ≥65 years for whom data existed on relevant sociodemographic and health variables over the four waves.

Diabetes complications (kidney, eye, and circulation problems) were self-reported in each wave through the specific questions on the potential consequence of diabetes. For example, each participant was asked: "As a result of your diabetes, have you ever had any problems with your kidneys?" The question was repeated for both the eye and circulation problems. Death information was from death certificates, National Death Index, and reports from family of subjects. The information from the National Death Index on underlying cause of death, as well as information on the cause of death collected from proxy, was used to identify diabetes-related deaths.

Consistency in use of diabetes medications

The use of diabetes medications was assessed by in-person interviews, using previously established protocols (20). A brief description of the protocols is as follows. In each wave, subjects were asked about use of the diabetic medications within 2 weeks of the assessment interview. Subjects were then asked to show the interviewer all the current prescription medications including oral hypoglycemics and insulin. Subjects were also asked if they actually took the medications in the 2 weeks before the interview. The interviewers documented the drug name, its dosage form, and strength. The generic equivalents of brand and fixed-dose combination diabetes medications were established. Subjects with inconsistent use of medication were those who, at any interview wave during the 7-year follow-up, *1*) discontinued their diabetes medications, *2*) did not use their diabetes medications within 2 weeks of the interview, or *3*) had no diabetic medications at home despite self-report of taking medicine for diabetes. Subjects with good consistency were those with consistent use of medication during the study period, and their diabetes medications were actually observed and documented by the in-home interviewers at all of the follow-up waves.

Independent factors

Factors potentially associated with consistent use of diabetic medication include sociodemographic variables (age, sex, marital status, years of formal education, household income, language of interview), medical insurance status (Medicare yes/no), supplemental health insurance (Medicaid yes/no; private/health maintenance organization [HMO] yes/no), medication type (only oral hypoglycemic versus insulin with or without oral hypoglycemics), activity of daily living (ADL) scale (21), instrumental ADL (IADL) scale (22), cognitive function, and depressive symptoms. Age was dichotomized to two groups to represent old (65–74 years) and very old (≥75 years) population. Because only 57.3% of subjects were born in the

U.S., the cutoff of ≤6 years of formal education was used to represent the population with primary or basic education. Also, because the majority of subjects had very low household income, the cutoff on $15,000 was arbitrary chosen.

ADLs included walking across a small room, bathing, grooming, dressing, eating, transferring from a bed to a chair, and using the toilet. Items on IADLs included using the telephone, taking medications, shopping for groceries or clothes, handling money, driving a car or being able to travel, doing heavy work around the house, walking up and down the stairs, and walking half a mile. Respondents were asked to indicate if they could perform these activities without help, if they needed help, or if they were unable to do them. No limitation was defined as needing no help, and any limitation was defined as needing help with or unable to perform one or more of the 7 ADLs or 10 IADLs.

Cognitive function was assessed with the 30-item Mini Mental State Examination (MMSE) (23). The English and Spanish versions of the MMSE, derived from the Diagnostic Interview Schedule (24), were used in this study. The scale has a potential range of 0–30 with lower scores indicating poorer cognitive function. MMSE score was used as a dichotomized variable (<21 vs. ≥21), which was a cutpoint frequently used for population with low average education (25,26). Depressive symptoms were assessed with the Center for Epidemiological Studies Depression (CESD) scale (27). The scale consists of 20 items that ask how often specific symptoms were experienced during the past week; responses were scored on a 4-point scale (scored 0–3) with potential total scores ranging from 0 to 60. The internal consistency of the scale was 0.89. A value of ≥16 was used to classify respondents as having high levels of depressive symptoms.

Statistical analysis

We examined sociodemographic, health characteristics, and diabetes complications for 908 diabetic subjects, stratified by inconsistency versus consistency in use of diabetes medication, using descriptive and univariate statistics for continuous variables and contingency tables (χ^2) for categorical variables. A multivariate logistic regression model was built to assess for predictors of inconsistency in use of diabetes medications, while simultaneously adjusting for all other confounding characteristics.

Additionally, logistic regression procedures and Cox proportional hazard model were used to assess risk of diabetes complications and death respectively by comparing subjects with poor consistency in use of diabetes medication with those with good consistency. For each complication, death, and diabetes-related death, two regression models were constructed—an unadjusted model and a model adjusted for additional variables of age, sex, medication type, years of diabetes, education, income, marital status, language of interview, insurance status, cognitive function, presence of depressive symptoms, ADLs, and IADLs. All analyses were done through the SAS System for Windows, Version 8.2.

RESULTS — Among the 908 diabetic subjects on prescribed medications and over four waves of assessment interviews, 148 discontinued their diabetes medications, 16 did not use their diabetes medications within 2 weeks of the interview, and 160 had no diabetic medications at home despite self-report of taking medicine for diabetes. Overall, 324 (36%) of diabetic subjects had inconsistent use of diabetes medications. The rates of inconsistency of drug usage between subjects on oral hypoglycemic drugs only and those on insulin (with or without oral hypoglycemic drug) were similar: 34% for the 461 subjects on oral hypoglycemic drugs only and 38% for the 447 subjects on insulin (with or without oral hypoglycemic drug).

Table 1 presents the percentage of inconsistency versus consistency of use of diabetic medications stratified by different subject characteristics. Table 2 presents the results of a multivariate analysis in which all of the characteristics were simultaneously evaluated for independent effect on inconsistent use of diabetic medications. In the multivariate logistic regression model, subjects who did not have Medicaid or private/HMO health insurance were significantly more likely to be inconsistent with treatment (OR 1.54, 95% CI 1.11–2.15 for Medicaid; 2.14, 1.22–3.76 for private/HMO). Additionally, subjects who were aged ≥75 years were significantly more likely to inconsistently use their diabetic medications (1.45, 1.03–2.04).

Table 3 presents the results of logistic regression models in predicting the risk of kidney, eye, and circulation problems by comparing the subjects with poor consistency in use of diabetic medication to those with good consistency, controlling for relevant confounders. There was a significant relationship between poor consistency in use of diabetic medications and risk of kidney problems. In the adjusted logistic regression models, subjects with inconsistent use of medication were more likely to report kidney problems (OR 1.59, 95% CI 1.13–2.23, $P = 0.008$) at follow-up compared with those who consistently used their medications, after controlling for relevant confounders such as age, sex, medication type, years of diabetes, education, income, marital status, language of interview, insurance status, cognitive function, presence of depressive symptoms, ADLs, and IADLs in the adjusted model. There was no significant difference in the risk of eye and circulation problems between subjects with inconsistent use of diabetes medications and those who were consistent with their medication usage.

Table 3 also shows the results of the Cox proportional hazard models predicting the risk of all-cause mortality and diabetes-related deaths by comparing subjects with poor consistency in use of diabetic medications with subjects with good consistency, adjusting for relevant confounders. In the adjusted Cox proportional model, inconsistent use of medication was found to increase the risk of death from any cause by 43% (HR 1.43, 95% CI 1.13–1.82, $P = 0.003$) and diabetes-related deaths by 66% (1.66, 1.20–2.30, $P = 0.002$) over a period of 7 years.

CONCLUSIONS — Our findings show that 36% of older Mexican Americans with diabetes were inconsistent in their use of prescribed diabetic medications. There was a significant association between supplemental health insurance and inconsistent use of diabetes medications among older Mexican Americans, after adjusting for relevant confounders. We also found a relationship between older age and irregular use of diabetic medications. Additionally, we found a significant relationship between inconsistency with diabetic medications usage and increased risk of kidney problems over a period of 7 years, controlling for age, sex, medication type, years of diabetes, education, income, marital status,

Table 1—*Characteristics associated with inconsistent use of diabetes medication*

Characteristics	*n*	Percentage with inconsistent use of diabetic medication	χ^2 *P* value
Age (years)			
65–74	642	33.5	0.032
≥75	266	41.0	
Sex			
Female	536	35.4	0.859
Male	372	36.0	
Education (years)			
≤6	663	36.6	0.474
>6	235	34.0	
Household income			
<$15,000	681	36.6	0.582
≥$15,000	189	34.4	
Marital status			
Married	533	34.7	0.465
Unmarried	375	37.1	
Language of interview			
English	184	35.3	0.910
Spanish	724	35.8	
Insurance type			
Medicare			
Yes	786	35.9	0.756
No	122	34.4	
Medicaid			
Yes	320	31.3	0.040
No	588	38.1	
Private/HMO			
Yes	94	23.4	0.009
No	814	37.1	
Depression			
CESD <16	614	36.2	0.482
CESD ≥16	211	38.9	
Cognition			
MMSE >21	597	35.9	0.456
MMSE ≤21	241	38.6	
ADL			
No limitation	722	36.7	0.206
Any limitation	183	31.7	
IADL			
No limitation	346	35.3	0.805
Any limitation	560	36.1	
Years of diabetes history			
≤5	280	31.4	0.276
6–10	200	39.5	
11–20	223	37.7	
>20	169	36.1	
Medication type			
Oral hypoglycemic	461	33.6	0.188
Insulin	447	37.8	

language of interview, insurance status, cognitive function, presence of depressive symptoms, ADLs, and IADLs. There were significant trends toward increased all-cause mortality and diabetes-related mortality in subjects with poor consistency in use of diabetic medications when compared with those with good consistency. Our study did not find any significant association between inconsistent use of diabetes medications and risk of eye and circulation problems.

The prevalence rate (36%) of inconsistent use of diabetes medications in our study was higher than rates reported in prior study for African-Americans (23.5%) and Caucasians (18%) (17). On the other hand, data from two recent studies of community-dwelling adults with type 2 diabetes showed higher rates (54–69%) of diabetes medications noncompliance compared with the rate we found (28,29). There are several possible explanations for these differences. For instance, our study, unlike the previous studies, examined rates of compliance, defined by consistency of use, for both oral hypoglycemic and insulin medications. Additionally, the wide variability in compliance rates reported in the literature can, in part, be due to differences in definition of medications adherence and in population sample (30–32). For example, Venter et al. (32), using presence of oral diabetes drugs in the urine as a measure of compliance in 68 African-American patients with type 2 diabetes, found a noncompliance rate of 65%. The rate in that study was almost two times as high as the rate we found among elderly Mexican Americans using self-reports of diabetes medications usage and verification of these medications by interviewers) (32).

Our findings on the relationship between insurance status and consistency in use of diabetes medications underscore the importance of access to sources that cover the cost of prescription medications. Medicaid and HMO insurances usually support drug benefits. Thus, lack of insurance that covers the cost of prescribed diabetes medications contributes to increased risk of inconsistency in use of diabetes medications. Conversely, Medicare insurance, which does not cover outpatient prescription drug, was not significantly associated with consistency in diabetes medication use. However, having access to insurance plans that pay for prescribed drugs does not necessarily lead to better diabetic control. For instance, Harris et al. (10) reported no significant relationship between having health insurance and level of glycemic control.

Past studies showed higher rates of diabetes complications (kidney, eye, and circulation problems and nontraumatic limb amputations) among diabetic Mexi-

Table 2—*Multivariate analysis in predicting inconsistent use of diabetes medication*

Characteristics	OR*	95% CI of OR*
Age		
65–74	1.000	
≥75	1.446	1.026–2.036
Sex		
Female	1.000	
Male	1.048	0.763–1.439
Education		
≤6	1.000	
>6	1.054	0.730–1.522
Household income		
<$15,000	1.000	
≥$15,000	0.865	0.596–1.254
Marital status		
Married	1.000	
Unmarried	1.053	0.758–1.462
Language of interview		
English	1.000	
Spanish	0.965	0.656–1.421
Insurance type		
Medicare		
Yes	1.000	
No	0.846	0.547–1.308
Medicaid		
Yes	1.000	
No	1.544	1.107–2.154
Private/HMO		
Yes	1.000	
No	2.139	1.219–3.755
Depression		
CESD <16	1.000	
CESD ≥16	1.050	0.736–1.500
Cognition		
MMSE >21	1.000	
MMSE ≤21	1.432	0.992–2.067
ADL		
No limitation	1.000	
Any limitation	0.783	0.514–1.193
IADL		
No limitation	1.000	
Any limitation	0.963	0.687–1.348
Years of diabetes history		
≤5	1.000	
6–10	1.056	0.693–1.610
11–20	0.976	0.641–1.485
>20	0.907	0.573–1.437
Medication type		
Oral Hypoglycemic	1.000	
Insulin	1.023	0.755–1.385

*OR from multivariable logistic regression model with all the characteristics in this table.

can Americans compared with diabetic non-Hispanic Caucasians of similar age (6,8–11). For instance, data from the San Antonio Heart Study showed a higher prevalence of kidney damage (proteinuria) among diabetic Mexican Americans compared with diabetic non-Hispanic Caucasians of similar age (8). One potential contributor to the higher prevalence of diabetes-related complications among diabetic Mexican Americans is the level of consistency with prescribed therapy. Prior studies showed that poor medications adherence is significantly associated with poor glycemic control, increased diabetes complications, and subsequent physical disability in older African-Americans and Caucasians (33,34). Our results extend these studies by showing the association of inconsistency in use of diabetic medications and increased risk of kidney problems and death over a 7-year period in a cohort of community-dwelling older Mexican Americans with diabetes.

Ascertainment of adherence to and consistency of use of medications in prior research ranged from self reports to more objective measures such as pharmacy refill records, medication monitors, and measurements of drug levels (30,35,36). There are some limitations to the definition of inconsistency of medication use in our study. First, we did not know the cause for inconsistent medication use by our subjects. It is probable that some subjects stopped their medications because of improvement of their diabetes or because of side effects related to the diabetic drugs. It is also conceivable that those who did not show their medications during the interviews could have them stored elsewhere. Second, we did not include data on drug-drug interactions and drug-disease interactions, potential reasons for therapeutically appropriate discontinuation of medications. Third, because the consistency of use of medication was only measured at each wave, the medication consistency status of the study participants, between interview waves and before the next assessment, was not known. For example, subjects who stopped their diabetic medication in the period between interviews but had the medications at the follow-up interview would be counted as having good consistency. Additionally, patients who needed multiple drug regimens for diabetes and responded affirmatively to "have you taken your diabetic medications in the last 2 weeks?" would be rated as consistent, even though the subject might only be taking one of the prescribed medications. Thus, we might have underestimated the prevalence of inconsistent use of diabetic medication in our study.

Next, the diagnosis of diabetes and diabetes complications was by self-report. However, prior research showed good

Table 3—*Prevalence of self-reported complications and risk of death among diabetic subjects with inconsistent and consistent use of diabetes medication*

Parameters	Poor consistency	Good consistency	Unadjusted model		Adjusted model†	
			OR/HR*	95% CI	OR/HR*	95% CI
Complications						
Kidney problems	89 (27.5)	114 (19.5)	1.562	1.136–2.147	1.588	1.130–2.231
Eye problems	165 (50.9)	316 (54.1)	0.880	0.671–1.155	0.790	0.590–1.059
Circulation problems	186 (57.4)	308 (52.7)	1.208	0.919–1.588	1.193	0.882–1.613
Mortality						
All deaths	133 (41.1)	181 (31.0)	1.383	1.105–1.730	1.434	1.132–1.816
Deaths from diabetes	75 (23.2)	88 (15.1)	1.599	1.175–2.176	1.664	1.202–2.304

Data are *n* (%) unless otherwise indicated. *OR from logistic regression and HR from Cox proportional hazard model; †adjusting all characteristics in Table 1.

agreement between self-reported diabetes and diabetes diagnosed by blood tests (37,38). Although self-reports of diabetes complications have been used extensively in large community-based studies (39–41), formal clinical evaluations for diabetic nephropathy, retinopathy, and peripheral vascular disease give the most accurate assessments of these complications. Nonetheless, most under-reporting associated with self-reports of diabetes complications, for instance as a result of recall bias or poor understanding of the complications, would likely lead to underestimation of risks of diabetes complications in our study.

Finally, given the sociodemographic heterogeneity of older Hispanics, our findings might not necessarily apply to other Hispanic elderly residing in the U.S. For instance, data from Hispanic-HANES 1982–1984 and 1988–1994 (6,7) showed that 15.8% of Cuban-Americans and 23.9% of Mexican Americans had diabetes, whereas non-Hispanic Caucasians had a rate of 11.2%. Despite these limitations, our source of data has several strengths, including its large community-based sample, 7 years of follow-up, and verification of the diabetic medications by the interviewers.

In conclusion, our study found that 36% of older diabetic Mexican Americans were inconsistent in the use of prescribed diabetes medications. Inconsistency in the use of diabetic medication was associated with increased risks of kidney problems and death over a 7-year period in this population. Intervention trials, such as the use of nurse-case management and culture-appropriate education materials, are needed to understand the optimal approach to better adherence, improved consistency with prescribed therapies, and better diabetes-related health outcomes among older Mexican Americans, which is one of the fastest growing ethnic groups in the U.S.

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