



ORIGINAL CONTRIBUTIONS

All-Cause and Cardiovascular Mortality among Mexican-American and Non-Hispanic White Older Participants in the San Antonio Heart Study—Evidence against the “Hispanic Paradox”

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Received for publication February 4, 2003; accepted for publication May 15, 2003.

The observation that Hispanics have lower all-cause and cardiovascular mortality rates despite increased rates of diabetes and obesity and lower socioeconomic status has been termed the “Hispanic paradox.” The authors therefore examined the relation between ethnicity and mortality in 1,438 Mexican-American and 921 non-Hispanic White San Antonio Heart Study participants, aged 45–64 years when they enrolled between 1979 and 1988. Over an average of 14.5 years, 466 deaths occurred: 238 attributed to cardiovascular disease (death certificate *International Classification of Diseases*, Ninth Revision, codes 401–414 or codes 420–447 with the exception of code 427.5) and 117 attributed to coronary heart disease (codes 410–414). Age- and gender-adjusted hazard ratios for all-cause, cardiovascular, and coronary heart disease mortality comparing Mexican Americans with non-Hispanic Whites were 1.50 (95% confidence interval (CI): 1.23, 1.81), 1.70 (95% CI: 1.30, 2.24), and 1.60 (95% CI: 1.09, 2.36), respectively. After adjusting for possible confounders, among diabetic individuals not using insulin, the authors found excess risk of all-cause, cardiovascular, and coronary heart disease mortality associated with being Mexican American; however, in nondiabetic individuals and insulin-using diabetic individuals, Mexican Americans and non-Hispanic Whites appeared to be at similar risk of mortality. Contrary to the prediction of the “Hispanic paradox,” in the San Antonio Heart Study, Mexican Americans were at greater risk of all-cause, cardiovascular, and coronary heart disease mortality than were non-Hispanic Whites.

cardiovascular diseases; cohort studies; coronary disease; diabetes mellitus, non-insulin-dependent; Mexican Americans; mortality; risk factors

Abbreviations: CI, confidence interval; HR, hazard ratio; ICD-9, *International Classification of Diseases*, Ninth Revision.

In the decade between 1990 and 2000, the US Hispanic population increased by more than 57.9 percent, becoming the fastest growing and largest minority group in the United States (1). In the year 2000, there were an estimated 35.3 million Hispanics, 12.5 percent of the total US population, with Mexican Americans being the largest ethnically distinct subgroup including 20.6 million people (1).

Despite Hispanics' higher rates of diabetes and obesity, lower socioeconomic status, and barriers to health care,

several studies have suggested that they have lower all-cause and cardiovascular mortality rates than do non-Hispanic Whites (2–10). Sociocultural factors have been invoked to explain this paradox; however, ethnic misclassification and differential ascertainment of deaths by ethnicity are alternative explanations (11–13). Recently, we published findings among diabetic participants of the San Antonio Heart Study indicating that, contrary to the prediction of the “Hispanic paradox,” US-born Mexican Americans were at greater risk

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while Mexican-born Mexican Americans appeared to be at similar risk of all-cause and cardiovascular mortality when compared with non-Hispanic Whites (14). However, because these findings were limited to individuals with diabetes, it remains unclear whether they extend to the general population. Therefore, we examined the relation between ethnic group and all-cause, cardiovascular, and coronary heart disease mortality in all San Antonio Heart Study participants between the ages of 45 and 64 years at baseline.

MATERIALS AND METHODS

The San Antonio Heart Study design and population

The San Antonio Heart Study cohort consists of 5,158 participants recruited at baseline in two phases: phase one between 1979 and 1982, and phase two between 1984 and 1988. Households were randomly sampled in three types of San Antonio neighborhoods: low-income, inner city, essentially 100 percent Mexican-American neighborhoods ("barrios"); middle-income, transitional neighborhoods; and high-income suburbs. Men and nonpregnant women between the ages of 25 and 64 years residing in the selected households were eligible and invited to participate. The combined response rate for both phases of the study was 65.3 percent. Details of the study design have been published previously (7, 15, 16). The Institutional Review Board of the University of Texas Health Science Center at San Antonio approved the study, and all subjects gave informed consent.

Baseline San Antonio Heart Study cohort examination

The baseline San Antonio Heart Study cohort examination was standardized and included interviews, blood pressure measurements, anthropometry, a fasting venipuncture, and an oral glucose tolerance test. Trained interviewers obtained information on demographic variables, medical history, medication use, and smoking status.

Ethnic group was defined by a validated algorithm that considered parental surnames and birthplaces, as well as the participant's preferred ethnic identity when a distinct national origin was indicated (15). Socioeconomic status was assessed by the participant's educational level (years) and the Duncan socioeconomic index (17, 18). Participants were asked to fast for at least 12 hours prior to their examination. Measurements of blood pressure, body mass index, total and high density lipoprotein cholesterol, triglycerides, and plasma glucose (fasting and 2 hours after a standardized oral glucose load) have been previously described (16, 19).

Prevalent Rose angina was ascertained using the London School of Hygiene Chest Pain Questionnaire (20). Prevalent heart disease, stroke, cancer, and gallbladder disease were defined on the basis of self-reported physician-diagnoses. A history of cardiovascular disease was defined as having had a heart attack, stroke, or Rose angina. A history of poor health was defined as having a history of cardiovascular disease, cancer, or gallbladder disease. Hypertension was defined as systolic blood pressure greater than or equal to 140 mmHg, diastolic blood pressure greater than or equal to 90 mmHg, or

current treatment with antihypertensive medication. Low high-density lipoprotein cholesterol was defined as less than or equal to 35 mg/dl (0.91 mmol/liter) in men and as less than or equal to 45 mg/dl (1.17 mmol/liter) in women. High total cholesterol was defined as greater than or equal to 240 mg/dl (6.22 mmol/liter). High triglycerides were defined as greater than or equal to 200 mg/dl (2.26 mmol/liter). Overweight was defined as a body mass index greater than or equal to 25 kg/m² and less than 30 kg/m², while obesity was defined as a body mass index greater than or equal to 30 kg/m². Diabetes was defined as fasting plasma glucose greater than or equal to 126 mg/dl (7.0 mmol/liter) and/or 2-hour postload glucose greater than or equal to 200 mg/dl (11.1 mmol/liter) (21). Participants not meeting these criteria but who self-reported physician-diagnosed diabetes and who reported current therapy with diabetes medication (either oral or insulin) were also considered to have diabetes. On the basis of self-reported medication use, diabetic participants were further classified into those using and not using insulin.

Study population, follow-up, and events

The current analyses are focused on San Antonio Heart Study participants aged between 45 and 64 years at enrollment into the study. Of the 2,362 San Antonio Heart Study participants who met these criteria, three individuals were excluded because we were unable to contact them after their baseline examination.

In 1999, a vital status follow-up of the San Antonio Heart Study cohort was initiated to determine all-cause and cause-specific mortality. Vital status was determined by annual mailed questionnaires, completed by a participant or next of kin. In cases of nonresponse, telephone interviews, home visits, voting records, driver registration, address information from the San Antonio Retail Merchants' Association, and the National Death Index were used to determine a participant's vital status. Among the 2,359 participants in this study, only nine people had incomplete vital status ascertainment through January 1, 2000 (eight Mexican Americans and one non-Hispanic White; ascertainment rate = 99.6 percent).

Information on cause of death was abstracted from death certificates (with names and ethnic identifiers suppressed) and sent to a certified nosologist (Medical Coding and Consultation Services, Rolesville, North Carolina) for coding according to the *International Classification of Diseases, Ninth Revision (ICD-9)*. Cardiovascular mortality was defined as deaths with the mention anywhere on the death certificate of ICD-9 codes 401–405 (hypertensive), 410–414 (ischemic), 420–429 (other) with the exception of code 427.5 (cardiac arrest), 430–439 (stroke), or 440–447 (arteries, etc.). Coronary disease mortality was defined as deaths with the mention anywhere on the death certificate of ICD-9 codes 410–414 (ischemic). Four deceased individuals without cause of death information were excluded from the cardiovascular and coronary heart disease mortality analyses.

Statistical analyses

Prospective analyses were carried out in which ethnicity determined a person's exposure status and all-cause, cardio-

vascular, or coronary heart disease mortality was the outcome.

Age- and gender-adjusted means and proportions were determined for participants' baseline characteristics stratified by ethnic group using regression methodology (22). For each ethnic group and all-cause, cardiovascular, and coronary heart disease mortality, Kaplan-Meier survival estimates were graphed over the follow-up period.

Cox proportional hazard models were used to calculate hazard ratios for all-cause, cardiovascular, and coronary heart disease mortality in relation to ethnicity. The association between ethnicity and all-cause, cardiovascular, and coronary heart disease mortality was then assessed after controlling for covariates and after excluding individuals with a history of cardiovascular disease or cancer. The covariates considered included age, gender, birthplace, diabetes status and insulin use (two index variables coded three categories: individuals without diabetes, individuals with diabetes not using insulin, and individuals with diabetes using insulin), hypertension status, histories of cardiovascular disease, cancer, and gallbladder disease, current smoking status, being overweight or obese, having high total cholesterol, having low high-density lipoprotein cholesterol, and having high triglycerides. For analyses including birthplace as a covariate, foreign-born non-Hispanic Whites were excluded, and two index variables coded three categories: non-Hispanic Whites, Mexican-born Mexican Americans, and US-born Mexican Americans. For each outcome, models with and without the appropriate interaction terms were compared to identify the interactions between significant covariates and ethnic group. A *p* value of 0.05 was used as a nominal value for statistically significant interactions. For each outcome, the assumption of proportional hazards was evaluated for significant covariates and the main exposure variable by testing for interaction with a continuous time variable. In cases of a significant violation of the assumption of proportional hazards (i.e., the time interaction variable had a *p* value < 0.05), results have been reported with respect to the first 10 years versus the remaining 10 years of the study.

RESULTS

The study population included 921 non-Hispanic Whites and 1,438 Mexican Americans between the ages of 45 and 64 years at enrollment into the San Antonio Heart Study. Participants were followed an average of 14.5 years. Prior to January 1, 2000, participants experienced a total of 466 deaths: 238 mentioning cardiovascular disease and 117 mentioning coronary heart disease on their death certificate.

At baseline, 43.5 percent of Mexican Americans were overweight, 34.8 percent were obese, 23.5 percent had diabetes, and 3.4 percent of the Mexican Americans required insulin for their diabetes, while 39.2 percent of non-Hispanic Whites were overweight, 18.3 percent were obese, 9.3 percent had diabetes, and 0.9 percent of the non-Hispanic Whites required insulin for their diabetes (table 1). Mexican Americans were also more likely to report cardiovascular disease and diabetes but less likely to report cancer than were non-Hispanic Whites. In addition, Mexican Americans had

lower levels of high density lipoprotein cholesterol and higher levels of triglycerides than did non-Hispanic Whites. For Mexican Americans and non-Hispanic Whites, unadjusted Kaplan-Meier survival estimates are illustrated for the follow-up period for all-cause, cardiovascular, and coronary heart disease mortality (figure 1).

The age- and gender-adjusted hazard ratio for all-cause mortality comparing Mexican Americans with non-Hispanic Whites was 1.50 (95 percent confidence interval (CI): 1.23, 1.81). Although diabetes status and insulin use, hypertension status, smoking status, a history of cardiovascular disease, and a history of cancer were independent predictors of all-cause mortality, birthplace, being overweight or obese, lipid levels, and a history of gallbladder disease were not. After controlling for these covariates as well as for age and gender, we found that the hazard ratio for all-cause mortality comparing Mexican Americans with non-Hispanic Whites remained above one and statistically significant (hazard ratio (HR) = 1.31, 95 percent CI: 1.07, 1.61) (table 2). Moreover, after excluding individuals with prevalent cardiovascular disease or cancer and controlling for the remaining covariates, we found that the hazard ratio for all-cause mortality comparing Mexican Americans with non-Hispanic Whites remained above one and statistically significant (HR = 1.34, 95 percent CI: 1.05, 1.71). Finally, after restricting the population to middle or high socioeconomic status participants (*n* = 1,524) and including the Duncan socioeconomic index, years of education, neighborhood, and the other previously included covariates, we found that the hazard ratio comparing Mexican Americans with non-Hispanic Whites though not statistically significant remained above one (HR = 1.24, 95 percent CI: 0.93, 1.65).

The age- and gender-adjusted hazard ratio for cardiovascular mortality comparing Mexican Americans with non-Hispanic Whites was 1.70 (95 percent CI: 1.30, 2.24). Although diabetes status and insulin use, hypertension status, smoking status, total and high density lipoprotein cholesterol levels, and a history of cardiovascular disease were independent predictors of cardiovascular mortality, birthplace, being overweight or obese, level of triglycerides, a history of cancer, and a history of gallbladder disease were not. After controlling for these covariates as well as for age and gender, we found that the hazard ratio for cardiovascular mortality comparing Mexican Americans with non-Hispanic Whites remained above one but was no longer statistically significant (HR = 1.30, 95 percent CI: 0.97, 1.75) (table 2). Moreover, excluding individuals with prevalent cardiovascular disease or cancer and controlling for the remaining covariates affected the hazard ratio for cardiovascular mortality comparing Mexican Americans with non-Hispanic Whites only slightly (HR = 1.34, 95 percent CI: 0.93, 1.92). Finally, after restricting the population to middle or high socioeconomic status participants (*n* = 1,500) and including the Duncan socioeconomic index, years of education, neighborhood, and the other previously included covariates, we found that the hazard ratio for cardiovascular mortality comparing Mexican Americans with non-Hispanic Whites remained above one (HR = 1.33, 95 percent CI: 0.88, 2.02).

The age- and gender-adjusted hazard ratio for coronary heart disease mortality comparing Mexican Americans with

TABLE 1. Characteristics (means or proportions and 95% confidence intervals) of the study population stratified by ethnicity among San Antonio Heart Study participants enrolled between 1979 and 1988 and followed for mortality from recruitment through January 1, 2000*

	Non-Hispanic White (<i>n</i> = 921)		Mexican American (<i>n</i> = 1,438)	
	No.	%	No.	%
	Unadjusted			
Age (years)	54.9		53.8	
Male	420	45.6	615	42.8
US born	893	97.0	1,179	82.0
Deceased before January 1, 2000	163	17.7	303	21.1
Cardiovascular mortality	77	8.4	161	11.2
Coronary heart disease mortality	39	4.2	78	5.4
	Adjusted for age and gender			
	%	95% CI†	%	95% CI
Diabetes	9.3	7.5, 11.3	23.5	21.3, 25.9
Using insulin for diabetes	0.9	0.5, 1.8	3.4	2.5, 4.5
Hypertension	25.7	22.8, 28.7	28.5	26.2, 31.1
Current smoker	27.4	24.5, 30.4	27.9	25.6, 30.4
Overweight: BMI, † 25–<30 kg/m ²	39.2	36.0, 42.5	43.5	40.9, 46.2
Obese: BMI, ≥30 kg/m ²	18.3	15.9, 21.0	34.8	32.3, 37.4
High total cholesterol	26.3	23.5, 29.3	24.7	22.5, 27.0
Low HDL‡ cholesterol	18.2	15.8, 20.9	27.0	24.8, 29.5
High triglycerides	21.5	18.9, 24.3	26.0	23.8, 28.4
Poor health‡	23.7	20.9, 26.6	26.5	24.2, 29.0
Cardiovascular disease history§	10.0	8.2, 12.2	13.4	11.6, 15.3
Cancer	10.2	8.3, 12.5	3.3	2.5, 4.4
Gallbladder disease	6.9	5.3, 8.9	15.0	12.8, 17.5
	Adjusted for age and gender			
	Mean	95% CI	Mean	95% CI
Duncan SEI† (scale: 0 (low)–100 (high))	61	59, 62	41	40, 42
Years of education	13.6	13.4, 13.9	9.1	8.9, 9.3
BMI (kg/m ²)	26.4	26.1, 26.8	29.0	28.7, 29.2
Fasting glucose (mg/dl)	95	92, 97	109	107, 111
2-hour glucose (mg/dl)	121	116, 127	165	160, 169
Systolic blood pressure (mmHg)	119	118, 120	124	123, 125
Diastolic blood pressure (mmHg)	72	72, 73	74	74, 75
Total cholesterol (mg/dl)	218	215, 220	215	213, 218
HDL cholesterol (mg/dl)	55	54, 56	50	49, 51
Triglycerides (mg/dl)	151	144, 158	173	167, 178

* Variables for which more than 1% of the population was missing information follow (number missing): birthplace (*n* = 9), diabetes (*n* = 36), hypertension (*n* = 3), history of cancer (*n* = 27), history of gallbladder disease (*n* = 97), Duncan socioeconomic index (*n* = 42), years of education (*n* = 33), fasting glucose (*n* = 40), 2-hour glucose (*n* = 174), total cholesterol (*n* = 31), high density lipoprotein cholesterol (*n* = 63), and triglycerides (*n* = 32).

† CI, confidence interval; BMI, body mass index; HDL, high density lipoprotein; SEI, socioeconomic index.

‡ Poor health was defined as having had cardiovascular disease, cancer, or gallbladder disease.

§ A history of cardiovascular disease was defined as having had a heart attack, stroke, or Rose angina.

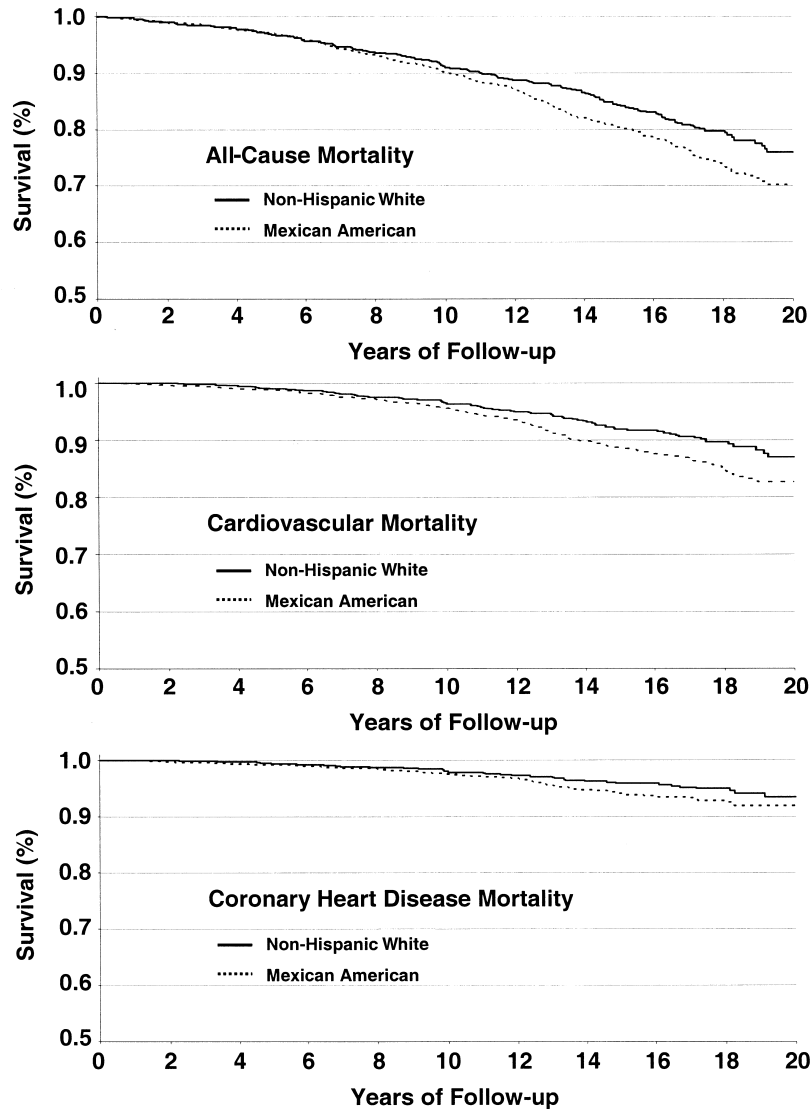


FIGURE 1. Unadjusted Kaplan-Meier all-cause, cardiovascular, and coronary heart disease survival estimates for older Mexican-American and non-Hispanic White San Antonio Heart Study participants recruited at baseline in two phases (phase 1: 1979–1982; phase 2: 1984–1988) and followed for mortality from recruitment through January 1, 2000.

non-Hispanic Whites was 1.60 (95 percent CI: 1.09, 2.36). Although diabetes status and insulin use, hypertension status, smoking status, total and high density lipoprotein cholesterol levels, and a history of cardiovascular disease were independent predictors of coronary heart disease mortality, birthplace, being overweight or obese, lipid levels, and a history of gallbladder disease were not. After controlling for these covariates as well as for age and gender, we found that the hazard ratio for coronary heart disease mortality comparing Mexican Americans with non-Hispanic Whites was about one (HR = 1.13, 95 percent CI: 0.74, 1.73) (table 2). Moreover, excluding individuals with prevalent cardiovascular disease or cancer and controlling for the remaining covariates affected the hazard ratio comparing Mexican Americans with non-Hispanic Whites only slightly

(HR = 1.08, 95 percent CI: 0.63, 1.86). Finally, after restricting the population to middle or high socioeconomic status ($n = 1,500$) and including the Duncan socioeconomic index, years of education, neighborhood, and other previously included covariates, the hazard ratio for coronary heart disease mortality comparing Mexican Americans with non-Hispanic Whites remained above one (HR = 1.20, 95 percent CI: 0.63, 2.27).

For each outcome after adjustment for significant covariates, there was evidence that diabetes status and insulin use modified the mortality differential between Mexican Americans and non-Hispanic Whites. Nondiabetic Mexican Americans and non-Hispanic Whites, as well as diabetic Mexican Americans and non-Hispanic Whites using insulin, appeared to be at similar risk of mortality, while diabetic Mexican

TABLE 2. Adjusted hazard ratios (and 95% confidence intervals) from multivariate Cox models for a given difference in risk factor level for all-cause, cardiovascular, and coronary heart disease mortality among San Antonio Heart Study participants enrolled between 1979 and 1988 and followed for mortality from recruitment through January 1, 2000*

	All-cause mortality (n = 2,293)		Cardiovascular mortality (n = 2,262)		Coronary heart disease mortality (n = 2,262)	
	Hazard ratio	95% CI†	Hazard ratio	95% CI	Hazard ratio	95% CI
Age (1-year increase)	1.10	1.08, 1.12	1.10	1.08, 1.13	1.10	1.06, 1.15
Gender (men vs. women)	1.73	1.43, 2.09	1.79	1.37, 2.33	2.05	1.39, 3.01
Ethnicity (Mexican Americans vs. non-Hispanic Whites)	1.31	1.07, 1.61	1.30	0.97, 1.75	1.13	0.74, 1.73
Diabetes status (diabetes mellitus) and insulin use						
Diabetes mellitus without insulin vs. no diabetes mellitus	1.95	1.57, 2.43	2.51	1.86, 3.39	2.72	1.77, 4.19
Diabetes mellitus with insulin vs. no diabetes mellitus	4.73	3.27, 6.85	7.11	4.43, 11.4	8.77	4.71, 16.3
Hypertension status (yes vs. no)	1.27	1.04, 1.54	1.62	1.23, 2.13	1.59	1.08, 2.36
Current smoker vs. others	1.95	1.61, 2.35	1.93	1.47, 2.54	1.50	1.00, 2.27
Total cholesterol (high vs. low)‡			1.45	1.09, 1.92	1.80	1.21, 2.69
HDL† cholesterol (low vs. high)§			1.54	1.14, 2.07	2.36	1.57, 3.55
Cardiovascular disease history (yes vs. no)	1.52	1.20, 1.92	1.92	1.41, 2.60	2.31	1.52, 3.51
Cancer history (yes vs. no)	1.55	1.10, 2.18				

* Covariates considered in the analyses that are not independent predictors of any outcome included birthplace, high triglycerides defined as ≥ 200 mg/dl (2.26 mmol/liter), being overweight or obese, and a history of gallbladder disease.

† CI, confidence interval; HDL, high density lipoprotein.

‡ High total cholesterol was defined as ≥ 240 mg/dl (6.22 mmol/liter).

§ Low HDL cholesterol was defined as 35 mg/dl (0.91 mmol/liter) or less in men and as 45 mg/dl (1.17 mmol/liter) or less in women.

Americans not using insulin appeared to be at higher risk of all-cause (HR = 1.94, 95 percent CI: 1.23, 3.06), cardiovascular (HR = 2.37, 95 percent CI: 1.25, 4.52), and coronary

heart disease (HR = 3.20, 95 percent CI: 1.12, 9.09) mortality than diabetic non-Hispanic Whites not using insulin (figure 2). Furthermore, among diabetic participants

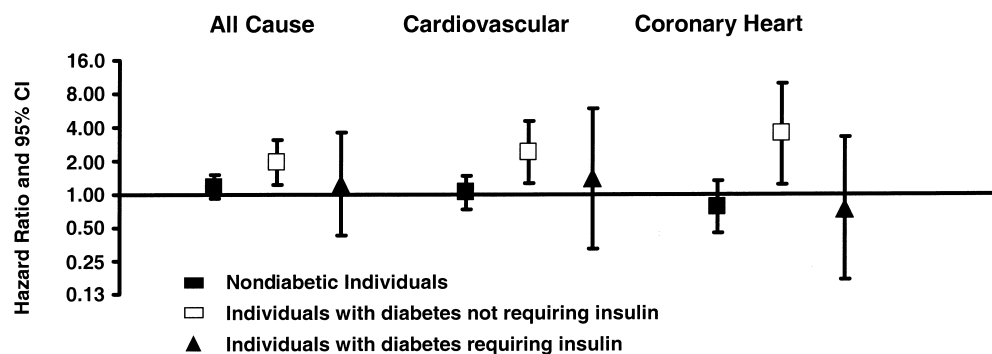


FIGURE 2. Cox hazard models predicting all-cause, cardiovascular disease, and coronary heart disease mortality in a San Antonio Heart Study comparison of Mexican Americans with non-Hispanic Whites stratified by diabetes/insulin use. Participants were recruited at baseline in two phases (phase 1: 1979–1982; phase 2: 1984–1988) and followed for mortality from recruitment through January 1, 2000. The all-cause model is adjusted for age, gender, hypertension status, smoking status, a history of cardiovascular disease, and a history of cancer. The cardiovascular disease model is adjusted for hypertension status, smoking status, total and high density lipoprotein cholesterol levels, and a history of cardiovascular disease. The coronary heart disease model is adjusted for hypertension status, smoking status, total and high density lipoprotein cholesterol levels, and a history of cardiovascular disease. Within each model appropriate interaction terms were used for stratification by diabetes/insulin use (all-cause, global: $p = 0.15$, interaction term for diabetics not requiring insulin: $p = 0.05$, interaction term for diabetics requiring insulin: $p = 0.92$; cardiovascular, global: $p = 0.09$, interaction term for diabetics not requiring insulin: $p = 0.03$, interaction term for diabetics requiring insulin: $p = 0.71$; coronary heart disease, global: $p = 0.04$, interaction term for diabetics not requiring insulin: $p = 0.01$, interaction term for diabetics requiring insulin: $p = 0.97$). CI, confidence interval.

TABLE 3. Age- and gender-adjusted characteristics (means and 95% confidence intervals) of individuals with diabetes stratified by ethnicity among San Antonio Heart Study participants enrolled between 1979 and 1988 and followed for mortality from recruitment through January 1, 2000

	Non-Hispanic White		Mexican American	
	Mean	95% CI*	Mean	95% CI
Participants not using insulin				
Fasting glucose (mg/dl)	136	123, 150	167	159, 174
2-hour glucose (mg/dl)	245	224, 266	310	299, 321
Duration of diabetes (years)	1.5	0.1, 2.9	3.9	3.2, 4.7
Participants using insulin				
Fasting glucose (mg/dl)	206	161, 251	201	161, 251
Duration of diabetes (years)	20.0	13.8, 26.1	15.7	13.1, 18.3

* CI, confidence interval.

not using insulin, the duration of diabetes and the fasting and 2-hour glucose levels were higher in Mexican Americans than non-Hispanic Whites, while among diabetic participants using insulin, the duration of diabetes and the fasting glucose levels were similar in Mexican Americans and non-Hispanic Whites (table 3). Further adjustment for the duration of diabetes slightly attenuated the higher all-cause (HR = 1.77, 95 percent CI: 1.12, 2.81) and cardiovascular (HR = 2.24, 95 percent CI: 1.17, 4.28) mortality but not the higher coronary heart disease (HR = 3.21, 95 percent CI: 1.13, 9.12) mortality in non-insulin-using Mexican Americans when compared with non-insulin-using non-Hispanic Whites, while the relations among nondiabetics and diabetics using insulin remained virtually unchanged.

With the exceptions of a history of cardiovascular disease being a stronger predictor of cardiovascular mortality and age being a weaker predictor of both cardiovascular and coronary heart disease mortality during the first 10 years of the study than in the remaining 10 years of the study, there was no evidence that the assumption of proportional hazards was violated.

Finally, sensitivity analyses were conducted for the outcomes of interest, assuming that missing information supported the "Hispanic paradox," that is, assuming the 11 Mexican Americans lost to follow-up were living as of January 1, 2000; the one non-Hispanic White lost to follow-up died a coronary heart disease death the day he or she was lost to follow-up; the two deceased Mexican Americans missing cause of death information did not die a cardiovascular death; and the two deceased non-Hispanic Whites missing cause of death information died from coronary heart disease. In the sensitivity analysis, the age- and gender-adjusted hazard ratio was reduced by less than 2 percent for all-cause mortality (HR = 1.48, 95 percent CI: 1.22, 1.79), was reduced by less than 3 percent for cardiovascular mortality (HR = 1.66, 95 percent CI: 1.26, 2.18), and was reduced by less than 8 percent for coronary heart disease mortality (HR = 1.48, 95 percent CI: 1.01, 2.16).

DISCUSSION

Contrary to postulates of the "Hispanic paradox," our results suggest that, after adjustment for age and gender, Mexican Americans are at increased risk of all-cause, cardiovascular, and coronary heart disease mortality relative to non-Hispanic Whites. Adjustment for biomedical risk factors, as well as for socioeconomic status, indicated that these factors accounted for some of the excess risk of all-cause, cardiovascular, and coronary heart disease mortality in Mexican Americans, but hazard ratios remained above one, providing further evidence against the "Hispanic paradox." Furthermore, there was evidence that diabetes status and insulin use modified the association between ethnic group and all-cause, cardiovascular, and coronary heart disease mortality. After adjustment for mortality risk factors, there were a twofold excess risk of all-cause and cardiovascular mortality and a threefold excess risk of coronary heart disease mortality associated with being Mexican American in individuals whose diabetes was not treated with insulin. Mexican Americans and non-Hispanic Whites without diabetes appeared to be at similar risk of mortality, as did Mexican Americans and non-Hispanic Whites whose diabetes was treated with insulin. Furthermore, among diabetic participants not using insulin, markers of disease severity, including duration and fasting and 2-hour glucose levels, were higher in Mexican Americans than non-Hispanic Whites, while among diabetic participants using insulin, markers of disease severity were similar in Mexican Americans and non-Hispanic Whites. These findings provide evidence that early diabetes, typically identified as less severe because it does not require insulin, is more severe and more deadly in Mexican Americans than in non-Hispanic Whites.

Ethnic misclassification and incomplete ascertainment of deaths may explain previous reports of a "Hispanic paradox" (11–13). Earlier studies typically used denominator information from the US Census with vital status information supplied from a state bureau of vital statistics, or they used the National Death Index to follow individuals participating

in national surveys (2, 3, 5, 6, 9). Studies that did not follow individuals over time but relied on aggregate data are likely affected by incomplete ascertainment of the population base and deaths within the population, as well as by differential ethnic misclassification with respect to the population base and observed deaths within the population. Moreover, biases introduced by studies that rely on aggregate data are likely to result in an underreporting of minority deaths, in this case Mexican-American deaths (23, 24). For example, failure to identify an individual as Hispanic on the death certificate reduces the total number of reported Hispanic deaths. Further, studies that did not verify vital status could suffer from differential incomplete ascertainment of deaths with respect to birthplace and ethnicity, again likely to underreport Mexican-American deaths. For example, individuals born outside the United States are more likely to leave the United States when they are no longer able to work or when they become seriously ill.

Historically, there have been explanations for the "Hispanic paradox" other than ethnic misclassification and differential ascertainment of deaths. Although currently a matter of debate, there is some evidence that certain groups of Native Americans, namely the Pima and Arizona Indians, have a lower than expected prevalence of coronary heart disease given their high prevalence of diabetes (25, 26); hence, admixture between Spanish and Native American populations in the hybrid Mexican-American population has been one explanation commonly given for the lower reported incidence of coronary heart disease in Mexican Americans compared with non-Hispanic Whites. However, there are at least two counterarguments. First, the low prevalence of coronary heart disease in the Pima Indians has been explained historically by their favorable lipid profile (25), but in our study population Mexican Americans have lower levels of high density lipoprotein cholesterol and higher levels of triglycerides than do non-Hispanic Whites. Second, the low prevalence of coronary heart disease is found only in some groups of Native Americans, American Indians from Oklahoma and North and South Dakota having been shown to be at a two- to threefold *increased* risk of coronary heart disease (26). Hence, given the heterogeneity of the American Indian populations and the known discrepancies between our population of Mexican Americans and the Pima Indians, even if we had found evidence in support of the "Hispanic paradox," Native American admixture among the Mexican-American population would have seemed an unlikely explanation.

Results from the present study are consistent with those from a community-based surveillance project, the Corpus Christi Heart Project, that has reported a higher incidence of hospitalized coronary heart disease among Mexican Americans than non-Hispanic Whites (27), a higher coronary heart disease fatality rate among Mexican Americans than non-Hispanic Whites (28, 29), and higher community-wide coronary heart disease mortality (both in and out of the hospital) in Mexican Americans than non-Hispanic Whites (30). A minor difference between the current study and the Corpus Christi Heart Project is that, in the latter, a statistically significant increased coronary heart disease mortality risk was reported in women, while a nonstatistically significant

increased coronary heart disease mortality risk was reported in men (30). In contrast, in the current study, there was no evidence that gender modified the association between ethnic group and all-cause, cardiovascular, or coronary heart disease mortality. Similar to our findings, those of the San Luis Valley Diabetes Study found that, in nondiabetic participants, there were no significant ethnic differences between Mexican Americans and non-Hispanic Whites in incident coronary heart disease, cardiovascular disease mortality, or coronary heart disease mortality; however, in direct contrast to our findings, the San Luis Valley Diabetes Study found that, in diabetic participants, Mexican Americans compared with non-Hispanic Whites were at lower rather than higher risk of incident coronary heart disease, cardiovascular disease mortality, and coronary heart disease mortality (8, 10). These differences could potentially be explained by either population differences or differences in the definition of the outcomes of interest. In the San Luis Valley Diabetes Study, medical records were reviewed to establish the "underlying" cause of death, while in the San Antonio Heart Study cardiovascular and coronary heart disease mortality were defined as "any mention" on the death certificate of cardiovascular or coronary heart disease mortality.

Finally, with two exceptions, results of the present study are consistent with our recently published findings concerning ethnic differences in mortality among diabetic participants of the San Antonio Heart Study (14). The first exception is that, among diabetic participants, we reported a difference in mortality risk between US-born Mexican Americans and Mexican Americans who immigrated to the United States. We postulated that the "healthy migrant effect" was one possible explanation for these differences and that, because earlier studies often lacked information on birthplace, differences in mortality risks according to birthplace may have contributed to the development of the "Hispanic paradox" theory. In the current study of participants aged 45–64 years, US-born Mexican Americans and Mexican-born Mexican Americans appeared to be at similar risk of all-cause, cardiovascular, and coronary heart disease mortality. The second exception is that, when the population was limited to diabetic San Antonio Heart Study participants, there was no evidence that insulin use modified the association between birthplace/ethnic group and mortality. We attribute this difference to the limited statistical power in the analysis of diabetic San Antonio Heart Study participants and the focus on birthplace.

This study is one of the first population-based cohort studies to follow Mexican-American and non-Hispanic White individuals over an extended time period, up to 20 years, for mortality. Although complete vital status ascertainment (>99 percent) was limited to San Antonio Heart Study participants aged 45–64 years at enrollment (46 percent of the original cohort), this study population includes the vast majority of San Antonio Heart Study participant deaths (86 percent of all known deaths given a 98 percent vital status ascertainment rate on the remaining cohort). Although the study population is representative of older individuals from each of the three types of neighborhoods from which it was selected, the response rate of 65.3 percent does not rule out the potential for selection bias that may influ-

ence external validity. The potential for ethnic misclassification was minimized because we defined a participant's ethnic group at baseline using a validated algorithm. Additionally, the potential cause-of-death misclassification differential with respect to ethnic group was limited to the completion of the death certificate, because the nosologist was masked to ethnic group. The high vital status ascertainment rates and the results of the sensitivity analysis, combined with the other strengths, make it unlikely that differential bias with respect to either exposure or outcome could explain our findings. Potential limitations of the study include the limiting of cardiovascular and coronary heart disease events to fatal events, as well as defining cause-specific mortality solely on the basis of death certificate information.

In summary, our study provides evidence against the "Hispanic paradox." Strictly speaking, our results apply only to Hispanics of Mexican origin, the principal Hispanic subgroup in San Antonio and the largest and fastest growing ethnically distinct subgroup of Hispanics in the United States. In contrast to the "Hispanic paradox," which would postulate that despite an unfavorable risk factor profile Mexican Americans compared with non-Hispanic Whites would have lower all-cause, cardiovascular, and coronary heart disease mortality, we found that age- and gender-adjusted hazard ratios indicate that Mexican Americans have a 50 percent greater risk of all-cause mortality, a 70 percent greater risk of cardiovascular mortality, and a 60 percent greater risk of coronary heart disease mortality than do non-Hispanic Whites. Adjustment for biomedical risk factors indicated that these factors accounted for the increased risk of mortality in individuals without diabetes and individuals with severe diabetes (i.e., diabetes requiring insulin) but not in individuals with less severe diabetes. Furthermore, these findings indicate that, in Mexican Americans, diabetes not requiring insulin has a potentially large public health impact, and that more aggressive measures are required to treat this disease.

ACKNOWLEDGMENTS

Grants from the National Heart, Lung, and Blood Institute (R01-HL24799 and R01-HL36820) supported this work. The research and writing of the manuscript were conducted under the sponsorship of both an American Heart Association Texas Affiliate Postdoctoral Fellowship and a National Research Service Award (T32-HL07446) from the National Heart, Lung, and Blood Institute. In addition, Dr. Hunt was partially supported by an American Diabetes Association Mentor-based Award.

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