

# Ethnic Disparities in Diabetic Complications in an Insured Population

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**I**N 1998, THE INITIATIVE TO ELIMINATE Racial and Ethnic Disparities in Health<sup>1</sup> proposed elimination of ethnic differences in diabetes and complications by 2010. Higher rates of microvascular complications, particularly end-stage renal disease (ESRD)<sup>2-4</sup> and lower extremity amputation (LEA),<sup>5</sup> were reported for blacks and Hispanics relative to whites with diabetes during the 1980s and early 1990s. However, more recent epidemiologic data detailing ethnic disparities in diabetes-related complications are lacking. It is unknown whether recent improvements in health care options for diabetes have benefited all groups equally or whether socioeconomic differences and substandard health care among minorities have continued to perpetrate differences noted in earlier studies. Disparate access to quality health care is a common explanation for ethnic disparities in diabetic complication rates in the US population.<sup>6</sup> When potential explanatory factors not related to health care (eg, genetic or innate physiological differences or behavioral factors) are studied, examining an ethnically diverse population with uniform health care coverage is useful. Few such studies of diabetes complications have been conducted. Here we report ethnic differences in the incidence of 5 major diabetic complica-

**Context** Higher rates of microvascular complications have been reported for minorities. Disparate access to quality health care is a common explanation for ethnic disparities in diabetic complication rates in the US population. Examining an ethnically diverse population with uniform health care coverage may be useful.

**Objective** To assess ethnic disparities in the incidence of diabetic complications within a nonprofit prepaid health care organization.

**Design and Setting** Longitudinal observational study conducted January 1, 1995, through December 31, 1998, at Kaiser Permanente Medical Care Program in northern California.

**Participants** A total of 62 432 diabetic patients, including Asians (12%), blacks (14%), Latinos (10%), and whites (64%).

**Main Outcome Measures** Incident myocardial infarction (MI), stroke, congestive heart failure (CHF), and nontraumatic lower extremity amputation (LEA), defined by primary hospitalization discharge diagnosis, procedures, or underlying cause of death; and end-stage renal disease (ESRD), defined as renal insufficiency requiring renal replacement therapy or transplantation for survival or by underlying cause of death.

**Results** Patterns of ethnic differences were not consistent across complications and frequently persisted despite adjustment for a wide range of demographic, socioeconomic, behavioral, and clinical factors. Adjusted hazard ratios (relative to that of whites) were 0.56, 0.68, and 0.68 for blacks, Asians, and Latinos, respectively ( $P < .001$ ), for MI; 0.76 and 0.72 for Asians and Latinos, respectively ( $P < .01$ ), for stroke; 0.70 and 0.61 for Asians and Latinos, respectively ( $P < .01$ ), for CHF; 0.40 for Asians ( $P < .001$ ) for LEA; and 2.03, 1.85, and 1.46 for blacks, Asians, and Latinos, respectively ( $P < .01$ ), for ESRD. There were no statistically significant black-white differences for stroke, CHF, or LEA and no Latino-white differences for LEA.

**Conclusions** This study confirms previous reports of elevated incidence of ESRD among ethnic minorities, despite uniform medical care coverage, and provides new evidence that rates of other complications are similar or lower relative to those of whites. The persistence of ethnic disparities after adjustment suggests a possible genetic origin, the contribution of unmeasured environmental factors, or a combination of these factors.

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tions observed in a 3-year longitudinal study of a diabetic population with uniform health care coverage.

## METHODS

### Study Cohort

Kaiser Permanente Medical Care Program (Kaiser Permanente), a fully integrated, nonprofit, group practice, prepaid health plan, provides comprehensive medical services to more than 2.9 million members (as of January 2000)

throughout northern California (including the San Francisco Bay and Sacramento metropolitan areas), or approximately 25% to 30% of the surrounding population. The Kaiser Permanente membership mainly includes employed individuals and closely approxi-

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mates the general population ethnically and socioeconomically, except for the extremes of the income distribution.<sup>7-9</sup>

In 1993, Kaiser Permanente established the Northern California Kaiser Permanente Diabetes Registry. The registry is updated annually by identification of all health plan members with diabetes from automated databases for pharmacy and laboratory information, hospitalization records, and outpatient diagnoses.<sup>10-19</sup> In 1996, registry sensitivity was estimated to be 96%, with a 2% false-positive rate. Between 1994 and 1996, all noninstitutionalized registry members who were 19 years or older and identified before January 1, 1996 (n=90 302), received a health survey (self-administered questionnaire) or a computerized telephone interview in English or Spanish. Eighty-three percent of eligible members with suspected diabetes completed the survey. After those who denied having diabetes or who discontinued membership in the health plan were excluded, 70 748 respondents with diabetes remained. The survey provided information on ethnicity (self-identified, allowing selection of more than 1 category), information needed to classify diabetes type (see Karter et al<sup>12</sup> for algorithm), diabetes family history, education, and behavioral risk factors. Analysis of ethnic variation in complication rates was restricted to the 62 432 survey respondents from the 4 major ethnic groups: black, 14%; Asian, 12%; Latino, 10%; and non-Latino white, 64%. Of those self-identified as Asian, 44% were Filipino; 24%, Chinese; 12%, Japanese; and 19%, Korean, other Asian, or mixed race. Those reporting other ethnic origin or mixed heritage were excluded because of insufficient sample sizes. Although we do not have race data for nonresponders, we compared the demographic composition (age, sex, and socioeconomic status) of diabetes survey responders to nonresponders in a previous study<sup>14</sup> and found no evidence suggesting responder bias. In addition to survey-derived data, we obtained measures of neighborhood-level SES by linking each member's address to the 1990

census block group-level average annual 1989 per capita income.

### Study End Points

We evaluated the incidence of 5 complications: myocardial infarction (MI), stroke (ischemic or hemorrhagic), congestive heart failure (CHF), nontraumatic LEA, and ESRD. The *International Classification of Diseases, Ninth Revision, Clinical Modification*<sup>20</sup> (ICD-9-CM) codes listed as either the primary hospitalization discharge diagnosis or the underlying cause of death on the death certificate were used to identify MI (ICD-9-CM code 410), stroke (ICD-9-CM codes 431, 433, 434, and 436), and CHF (ICD-9-CM codes 402.01, 402.11, 402.91, and 428). The LEA procedures were identified from discharge codes (ICD-9-CM procedure codes 84.10-84.17). End-stage renal disease was identified from Kaiser Permanente's ESRD treatment registry or defined by chronic renal failure listed as the underlying cause of death on the death certificate (ICD-9-CM codes 250.4, 403-404, 585, and 586). Emergency events serviced by non-Kaiser Permanente hospitals were captured via a claims reimbursement database for outside medical services. Mortality and cause of death were ascertained with a validated program, the California Automated Mortality Linkage System.<sup>21</sup>

Previous studies have validated these end points in this population. For MI, 584 (98.7%) of a sample of 602 hospital discharge diagnoses also had a chart-confirmed acute MI based on consistent symptoms, elevated cardiac enzyme levels, or diagnostic electrocardiographic changes (A. Go, oral communication, September 2000). For CHF,<sup>11</sup> 194 (97%) of 200 cases met either the major or minor criteria for heart failure.<sup>22</sup> In a previous Kaiser Permanente study of ischemic stroke (ICD-9-CM codes 433.00-434.91 and 436.0), 627 (75%) of a consecutive sample of 836 hospitalizations with 1 of these codes as a primary discharge diagnosis were validated by chart review by using a strict definition of documented spontaneous neurologic deficit lasting longer than 24 hours, with no evidence of trauma or

other competing nonvascular origin (A. Go, oral communication, September 2000). However, the modest validation rate in that study was attributable to inclusion of stroke patients who were in skilled nursing or long-term care facilities and were hospitalized for stroke rehabilitation, whereas our study would have excluded these prevalent cases. In 2 separate validations of LEA (A.J.K., unpublished data, 2000, n=109; Selby and Zhang,<sup>23</sup> n=209), 99% of electronic hospital discharge records were confirmed by chart review. Data from Kaiser Permanente's ESRD treatment registry are transferred directly to the Centers for Medicare and Medicaid Services United States Renal Data System and to Medicare for reimbursement. Given the federally mandated certification of all ESRD treatment records, we assume a high level of validity.

### Statistical Analysis

We used a follow-up study to evaluate the incidence of each complication. Baseline was defined as January 1, 1995, for all members surveyed in 1994 and the survey date (January 1995 to March 1997) for those surveyed after that date. The duration of follow-up (person-time) was tabulated through membership records and ended with an event, censoring because of dropping of Kaiser Permanente membership for any period longer than 2 months, death, or the end of the study (December 31, 1998). For analyses of complications other than ESRD, we excluded those with a history of events of the same type noted in hospital discharge records during the 5 years before baseline. The ESRD treatment registry contains lifetime histories of renal dialysis and transplantations, allowing us to exclude all prevalent ESRD cases. All prognostic, confounding, and stratifying variables were ascertained at or before baseline from automated records, the diabetes survey, and the 1990 census.

### Descriptive and Multivariate Analysis

Using direct standardization with the entire diabetes cohort as the population

standard, we calculated age-adjusted and sex- and ethnic-specific rates for each complication with SAS version 8 (SAS Institute Inc, Cary, NC). Proportional hazards regression (Cox) models were then used to calculate adjusted hazard ratios (HRs) as an estimate of the relative risk for Asians, blacks, and Latinos relative to whites (reference group), allowing for censored data. Because the relationship between ethnicity and each complication did not differ statistically by sex (all sex-ethnic cross-product terms  $P > .10$ ), we pooled the data for men and women. Additionally, we found no violations of the proportionality assumption. We then specified a series of Cox regression models: a base, a demographic model (age and sex adjusted), and 3 additional models, which added groups of related, potentially explanatory variables to the base model only. The SES model added individual-level education and average census block-level income to the demographic model. The modifiable risks model added smoking status, alcohol intake, self-reported treatments for diabetes (including diet and exercise), frequency of self-monitoring of blood glucose levels, and obesity status based on body mass index<sup>24</sup> to the demographic model. Finally, the clinical model added characteristics specific to diabetes to the demographic model, including type of diabetes, diabetes duration (ie, time since diagnosis), diabetes therapy, and first-degree family history of diabetes. Two additional risk factors were added for amputation only, height<sup>25,26</sup> and peripheral neuropathy.<sup>23,27</sup> We then specified fully adjusted models to assess the combined explanatory effect of all of these factors (see TABLE 1 for cut points for each categorical variable).

## RESULTS

### Population Characteristics

The study population of 62 432 included 8496 black patients (14%), 7632 Asian patients (12%), 6279 Latino patients (10%), and 40 025 white patients (64%) with diabetes followed up for approximately 135 000 person-years (approximately 2.5 years per

member). Baseline characteristics are detailed in Table 1. Latinos were least likely (36%) and Asians were most likely (67%) to have more than a high school education. Blacks and Latinos were at least twice as likely as Asians and whites to live in a census block with more than one fifth of families earning below the poverty level or with at least a two-thirds majority employed in working-class occupations. Type 1 diabetes mellitus was more than twice as common among whites relative to the

other groups. Blacks were most likely to treat their diabetes with insulin and least likely to control their diabetes without pharmacotherapy. Of those with type 2 diabetes mellitus, Asians had the shortest duration of diabetes and were least likely to be treated with insulin. Latinos were least likely to self-report using diet and exercise as a component of their treatment for diabetes even though they were as likely (21%) as Asian and whites (22%) to control their diabetes without pharmaco-

**Table 1.** Baseline Characteristics for 62 432 Black, Asian, Latino, and White Patients With Diabetes\*

	Black (n = 8496)	Asian (n = 7632)	Latino (n = 6279)	White (n = 40 025)
Age, mean (SD), y	58.8 (12.6)	57.0 (11.9)	56.7 (12.3)	61.0 (13.1)
Women	52	46	48	45
Educational attainment				
High school or less	45	33	65	43
Some college	37	24	24	32
College graduate	18	43	12	25
Lives in working-class neighborhood†	60	44	61	39
Lives in economically disadvantaged neighborhood‡	30	8	16	6
Diabetes type				
Type 1	3	2	3	7
Type 2				
Insulin§	27	14	20	21
Oral agents only	54	62	57	51
No pharmacological therapy	16	22	21	22
Reported diet as part of treatment	54	57	51	60
Reported exercise as part of treatment	49	53	43	47
Daily self-monitoring of blood glucose level	30	20	25	34
HbA <sub>1c</sub> level, mean (SD)	8.9 (1.8)	8.7 (1.8)	8.8 (2.0)	8.4 (1.8)
Poor glycemic control (HbA <sub>1c</sub> level >10%)	28	22	27	18
First-degree family history of diabetes	65	58	74	51
Duration of diabetes (<10 y)	59	70	63	62
Antilipemic treatment use	10	15	9	14
Antihypertensive treatment use	65	50	45	58
Self-reported hypertension	71	59	55	62
Self-reported peripheral neuropathy	32	19	31	32
Body mass index, mean (SD), kg/m <sup>2</sup>	30.9 (6.4)	25.8 (4.3)	30.3 (6.1)	30.0 (6.6)
Obesity status (kg/m <sup>2</sup> )				
Underweight (<18.5)	1	1	0.5	1
Normal (18.5-24.9)	15	46	16	21
Overweight (25.0-29.9)	36	39	40	36
Obesity class 1 (30.0-34.9)	27	11	25	24
Obesity class 2 (≥35.0)	21	3	19	19
Alcohol intake (>21 drinks/wk)	3	1	4	3
Current smoker	16	8	11	12

\*Subjects older than 19 years are considered adults. Data are presented as percentages unless otherwise indicated and may not total 100% because of rounding.

†Indicates that more than 66% in the census block group are in a working-class occupation.

‡Indicates that more than 20% of the neighborhood's population has an annual income below poverty level.

§Includes those receiving insulin monotherapy and those receiving insulin in combination with oral agents.

therapy. Whites had the lowest mean hemoglobin A<sub>1c</sub> level at baseline and were most likely to report daily self-monitoring of blood glucose levels. First-degree family history of diabetes was most common in Latinos, intermediate in blacks and Asians, and least common among whites. Antilipemic treatment was most common among Asians and whites. Antihypertensive treatment and self-reported hypertension were most common among blacks and whites. Asians stood out as having substantially lower rates of self-reported peripheral neuropathy, obesity, current smoking, and heavy drinking than the other 3 ethnic groups.

### Myocardial Infarction

We identified 1751 individuals who experienced a first MI during follow-up. Age-adjusted incidence was higher (by 30%-70%) in men relative to women across all ethnic groups (TABLE 2).

Blacks, Asians, and Latinos had 34%, 32%, and 26% lower age- and sex-adjusted incidence of MI relative to whites, respectively. These differences persisted despite separate and combined adjustment for socioeconomic factors, modifiable risk factors and self-care behaviors, and diabetes-related clinical traits (FIGURE). Adjusted hazard ratios relative to those of whites (with 95% confidence intervals [CIs]) were as follows: black, 0.56 (0.47-0.66;  $P < .001$ ); Asian, 0.68 (0.57-0.82;  $P < .001$ ); and Latino, 0.68 (0.56-0.81;  $P < .001$ ).

### Stroke

There were 1493 individuals who experienced a first stroke during follow-up. Incidence rates were similar in men and women belonging to the same ethnic group. Relative to whites, blacks had a 20% higher age- and sex-adjusted rate of stroke ( $P = .01$ ). Further adjustment, es-

pecially for diabetes-related clinical traits, attenuated the HR for blacks, resulting in a nonsignificant black-white difference. Asians and Latinos had 24% ( $P < .001$ ) and 18% ( $P = .03$ ) lower sex- and age-adjusted incidence rates, which remained significantly lower than that of whites, with simultaneous adjustment for the risk factor domains. Adjusted hazard ratios relative to that of whites (95% CI) were as follows: black, 1.04 (0.89-1.22;  $P = .61$ ); Asian, 0.76 (0.62-0.93;  $P = .008$ ); and Latino, 0.72 (0.59-0.88;  $P < .002$ ).

### Congestive Heart Failure

During follow-up, there were 1307 hospital admissions or deaths caused by CHF. Age-adjusted incidence was not significantly different between men and women. Relative to whites, Asians and Latinos had a 36% ( $P < .001$ ) and 32% ( $P < .001$ ) lower age- and sex-adjusted CHF incidence, respectively. Age- and

**Table 2.** Incidence Rates for Fatal and Nonfatal Myocardial Infarction, Stroke, Congestive Heart Failure, End-Stage Renal Disease, and Lower Extremity Amputation Procedures

	Total Person-Years of Follow-up	Incident Events, No.	Age- and Sex-Adjusted Incidence Rate per 1000 Person-Years (95% Confidence Interval)	Age-Adjusted Incidence Rate per 1000 Person-Years (95% Confidence Interval)	
				Women	Men
<b>Myocardial infarction</b>					
Black (n = 8126)	17 106	158	9.1 (7.7-10.6)	6.6 (5.1-8.4)	11.1 (9.0-13.6)
Asian (n = 7362)	15 880	145	9.3 (7.8-11.0)	6.6 (4.8-8.8)	11.7 (9.5-14.2)
Latino (n = 5991)	13 934	138	10.1 (8.5-12.0)	7.8 (5.8-10.4)	12.0 (9.6-14.9)
White (n = 37 161)	82 951	1310	13.7 (13.0-14.5)	11.9 (10.9-13.0)	15.3 (14.2-16.5)
<b>Stroke</b>					
Black (n = 8263)	17 358	218	11.8 (10.3-13.5)	12.7 (10.5-15.1)	11.0 (8.9-13.4)
Asian (n = 7462)	16 111	117	7.4 (6.1-9.0)	7.0 (5.1-9.3)	7.8 (6.0-10.0)
Latino (n = 6158)	14 334	109	8.0 (6.5-9.7)	7.9 (5.8-10.5)	8.0 (6.0-10.4)
White (n = 38 744)	86 649	1049	9.8 (9.2-10.4)	9.3 (8.4-10.2)	10.2 (9.3-11.0)
<b>Congestive heart failure</b>					
Black (n = 8013)	16 895	192	10.7 (9.2-12.3)	10.3 (8.4-12.6)	11.0 (8.9-13.4)
Asian (n = 7402)	16 023	93	5.9 (4.7-7.2)	4.2 (2.9-6.0)	7.3 (5.6-9.4)
Latino (n = 6068)	14 173	87	6.3 (5.0-7.8)	5.9 (4.2-8.1)	6.7 (4.9-9.0)
White (n = 37 498)	84 365	935	9.2 (8.6-9.9)	9.5 (8.6-10.4)	9.1 (8.3-9.9)
<b>Lower extremity amputation</b>					
Black (n = 8378)	17 640	82	4.7 (3.7-5.9)	2.8 (1.9-4.1)	6.5 (4.8-8.5)
Asian (n = 7605)	16 512	23	1.5 (0.9-2.3)	1.2 (0.6-2.3)	1.7 (0.8-3.1)
Latino (n = 6211)	14 502	56	3.8 (2.9-5.0)	2.7 (1.6-4.2)	4.9 (3.4-6.8)
White (n = 39 574)	88 916	413	4.2 (3.8-4.7)	3.0 (2.5-3.6)	5.3 (4.6-6.0)
<b>End-stage renal disease</b>					
Black (n = 8364)	17 584	127	6.8 (5.7-8.1)	8.0 (6.3-10.1)	5.7 (4.2-7.5)
Asian (n = 7540)	16 336	77	4.6 (3.6-5.8)	3.7 (2.5-5.4)	5.4 (4.0-7.1)
Latino (n = 6202)	14 481	66	4.5 (3.5-5.8)	4.4 (3.0-6.3)	4.6 (3.2-6.3)
White (n = 39 683)	89 348	281	3.2 (2.8-3.6)	2.8 (2.3-3.4)	3.5 (3.0-4.2)

sex-adjusted rates for blacks were higher but not significantly different than those for whites; however, adjustment for diabetes-related clinical traits attenuated the HR for blacks. Other disparities were not altered substantially by separate or combined adjustment for risk factor domains. Adjusted hazard ratios relative to that of whites (95% CI) were as follows: black, 0.93 (0.79-1.10;  $P=.39$ ); Asian, 0.70 (0.56-0.87;  $P<.001$ ); and Latino, 0.61 (0.48-0.76;  $P<.001$ ).

### Nontraumatic LEA

During follow-up, there were 574 hospitalizations with LEA procedures. For blacks and whites, age-adjusted incidence rates were significantly higher in men than women. Age- and sex-adjusted incidence rates of LEA did not differ significantly between whites and blacks or Latinos, whereas Asians had a rate 64% lower than that of whites ( $P<.001$ ). Adjustment for diabetes-related clinical traits again attenuated the HR for blacks. The substantially lower rates of amputation among Asians persisted despite separate and combined adjustment for risk factor domains. Adjusted hazard ratios relative to that of whites (95% CI) were as follows: black, 0.84 (0.65-1.08;  $P=.16$ ); Asian, 0.40 (0.28-0.62;  $P<.001$ ); and Latino, 0.85 (0.63-1.14;  $P=.27$ ).

### End-Stage Renal Disease

During follow-up, there were 551 individuals with newly initiated ESRD treatments or deaths caused by renal failure. Age-adjusted incidence rates did not differ significantly between men and women from the same ethnic group. Relative to that of whites, age- and sex-adjusted incidence rates of ESRD were significantly higher for blacks, Asians, and Latinos (112% [ $P<.001$ ], 44% [ $P<.001$ ], and 41% [ $P=.004$ ] higher, respectively;  $P<.004$ ). For each ethnic group, relative to whites, HR estimates remained significantly higher than unity despite separate and combined adjustment for risk factor domains. Adjusted hazard ratios relative to that of whites (95% CI) were as fol-

lows: black, 2.03 (1.62-2.54;  $P<.001$ ); Asian, 1.85 (1.40-2.43;  $P<.001$ ); and Latino, 1.46 (1.10-1.93;  $P=.004$ ).

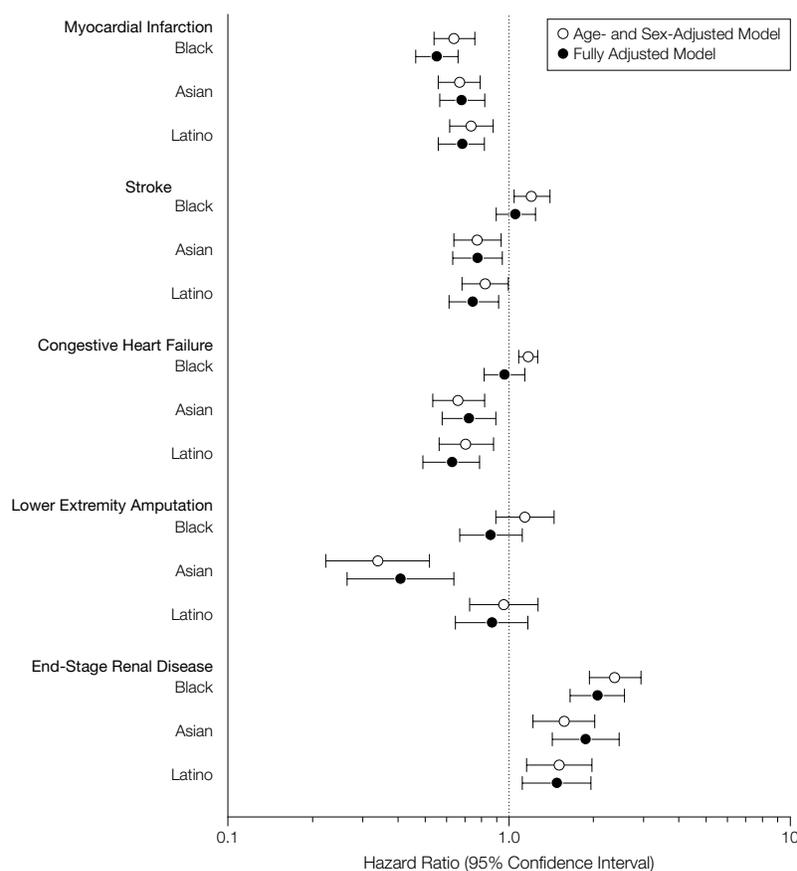
### COMMENT

In a large diabetic cohort with uniform health care coverage, we found ethnic disparities in the incidence of each of the most debilitating and costly diabetic complications. In models adjusted for demographics, socioeconomic, behavior, and clinical profile, relative to whites, Asians and Latinos had significantly lower cardiovascular disease rates (MI, CHF, and stroke), and

blacks also had significantly lower incidence of MI but had the same incidence of CHF and stroke as whites. The incidence of LEA procedures among Asians was one third that of whites, whereas rates for blacks and Latinos did not differ significantly from that of whites. All 3 minority ethnic groups had significantly higher incidence of ESRD than whites. However, ethnic disparities for LEA and ESRD observed in this insured population with diabetes were usually smaller than those reported in previous population-based studies.

Our findings of lower rates of MI were

**Figure.** Hazard Ratios and 95% Confidence Intervals for Ethnicity (Reference: Whites) From Cox Proportional Hazard Models of Diabetic Complications



Hazard ratios and 95% confidence intervals (error bars) are shown for ethnicity (reference, whites) from Cox proportional hazard models of myocardial infarction, stroke, congestive heart failure, end-stage renal disease (fatal or nonfatal), and nontraumatic lower extremity amputation. The fully adjusted model includes ethnicity, age, sex, individual-level educational attainment, census block group-level annual income and proportion of neighborhood with working-class occupations, smoking status, alcohol intake, frequency of self-monitoring of blood glucose levels, exercise reported as a treatment for diabetes, obesity status based on body mass index according to the current<sup>23</sup> classification of overweight and obesity, first-degree family history of diabetes, duration of diabetes (ie, time since diagnosis, type of diabetes, diabetes therapy), and height (for amputation only).

consistent with that of national surveillance reports<sup>28,29</sup> and population-based studies<sup>30-32</sup> that reported lower risks of coronary heart disease among ethnic minorities with diabetes, particularly blacks and Latinos. However, few published data exist for Asians, and no data on ethnic differences in CHF among persons with diabetes exist. In contrast to our findings and those from a study in the United Kingdom,<sup>33</sup> most studies<sup>28,34,35</sup> have reported substantially higher rates of LEA among blacks relative to whites (relative risks, 1.8-2.3). Our finding of similar LEA rates among Latinos and whites is consistent with 1 report.<sup>5</sup> Additionally, our observation of a substantially lower LEA rate among Asians is consistent with a single report from the United Kingdom of a 4-fold lower incidence of LEA in diabetic South Asians relative to European whites.<sup>36</sup> The 2.5- and 1.5-fold higher incidence of ESRD among blacks and Latinos relative to whites is consistent with nationwide<sup>28</sup> and some state surveillance reports,<sup>2,37</sup> although much larger minority excesses have been reported in some regional studies (eg, 6.5- and 6.1-fold higher incidence in Texas).<sup>38</sup> Recent published reports on the incidence of ESRD among Asians with diabetes relative to other ethnic groups in the United States are unavailable, although an excess burden in Asians relative to whites living in the United Kingdom has been confirmed.<sup>39</sup>

### Explanatory Factors

Minority excesses in adverse health outcomes are likely due in part to lower SES, disproportionate enrollment in health plans with poorer performance,<sup>40</sup> and associated reductions in access to quality health care caused by lack of health insurance or less comprehensive coverage.<sup>6,41-47</sup> Uninsured individuals are less likely to seek medical care after being newly diagnosed as having diabetes,<sup>48</sup> possibly resulting in more rapid disease progression. A recent national study<sup>49</sup> (1997-1999 Behavioral Risk Factor Surveillance System survey) reported reduced levels of several processes of diabetes care among Latinos relative to other

ethnic groups surveyed. There is also some evidence from other populations that minorities receive inferior medical care despite having health coverage.<sup>50-54</sup> A recent study of the quality of care for Medicare beneficiaries enrolled in managed care reported that blacks with diabetes were significantly less likely to receive retinal examinations than whites.<sup>40</sup>

Given previously reported associations between SES and diabetes-related outcomes<sup>55-58</sup> and our observations of ethnic differences in SES and significantly lower incidence of each complication among college graduates (data not shown), we expected SES disparities to explain a substantial portion of the unadjusted ethnic differences. Contrary to expectation, age- and sex-adjusted model estimates of ethnic differences did not differ substantively from estimates additionally adjusted for an individual's education and 2 census block-level variables (neither significantly related to complications), average annual income and proportion in working-class occupations in their neighborhood. The SES effect is likely diminished in fully insured populations such as this study population in which comprehensive health coverage removes most financial barriers to health care.

Modifiable behavioral variables (self-reported smoking status, alcohol consumption, body mass index, home glucose monitoring frequency, and exercise and diet as a self-reported treatment for their diabetes) also failed to explain ethnic variation. For ethnic groups other than blacks, differences in clinical profile (duration of diabetes, first-degree family history of diabetes, type and therapy for diabetes, and peripheral neuropathy) explained relatively little of the observed ethnic differences in complication rates. Among blacks, adjusting for clinical profile tended to attenuate the HR for stroke, CHF, and LEA. Consistent with those of previous studies, height ( $P < .001$ )<sup>25,26</sup> and peripheral neuropathy ( $P < .001$ )<sup>23,27</sup> were significantly related to the risk of LEA in our population. Among Asians, average height (1.63 m) and the prevalence of peripheral neuropathy (19%)

were significantly lower than among blacks, Latinos, and whites (height: 1.71, 1.66, and 1.71 m, respectively;  $P < .001$ ; and peripheral neuropathy: 32%, 31%, and 32%, respectively;  $P = .001$ ). However, the markedly lower rate of LEA among Asians was not explained by their more favorable profile of established risk factors.

The patterning of ethnic disparities across the range of complications within a single health care environment is itself informative. Although some differences in access to relevant components of preventive health care may persist across ethnic groups, even in a setting of uniform insurance coverage, one would expect poorer care to increase the risk of each complication for the disadvantaged ethnic group. Additionally, healthy lifestyle behaviors that reduce disease progression (eg, weight control and exercise) are likely to be beneficial for each complication and ethnic group. Thus, one would expect that, for a given ethnic group, if either inadequate preventive care or poor health behaviors explained elevated relative rates of a specific complication, then similar elevations should be observed across all complications. Instead, we found no consistency in the ethnic rankings across complications. For example, whites had the highest incidence of MI but the lowest of ESRD, blacks had the lowest incidence of MI but the highest of ESRD, Asians and Latinos had intermediate rates for MI and ESRD, and Asians differed substantially from the other 3 groups by having much lower LEA rates.

Because residual disparities remain in the fully adjusted models, there must exist some key explanatory factors not specified in these models that account for the disparities. Psychosocial stressors and attitudes,<sup>59</sup> diabetes knowledge and medical literacy,<sup>60</sup> adherence and service use,<sup>61</sup> and physician perceptions and racial discrimination<sup>62-64</sup> have been proposed as causes of ethnic disparities. However, analogous to health care and behaviors, ethnic differences in these internal and external environmental factors are more

likely to result in consistent direction of effects across complications rather than the variable patterns we observed. Ethnic differences in genetic susceptibility are a plausible alternative explanation for the persistent inconsistency we observed across populations. For example, there is evidence for a genetic basis for the greater familial aggregation of renal disease among blacks.<sup>65,66</sup> However, our observations provide evidence of a genetic origin by default only and thus should be considered strictly suggestive; further direct study of the ethnic differences in the genetics of diabetes-related complications is needed.<sup>67</sup>

Competing risk for mortality has also been suggested as a potential promoter of ethnic disparities. Despite an often earlier onset of diabetes, lower rates of coronary heart disease among diabetic Latinos<sup>30</sup> may confer longer survival relative to that of whites and thus a greater opportunity for Latinos to express microvascular complications such as ESRD or LEA. However, this hypothesis was not supported by our observations. The average age at death among our diabetic cohort was oldest for whites (72.0 years), youngest for Latinos (68.8 years), and intermediate for blacks (69.9 years) and Asians (69.3 years). Additionally, although elevated rates of ESRD among the minority groups with lower MI rates support this hypothesis, the higher LEA rates for whites do not.

The attenuated ethnic disparities observed in our study could conceivably be attributable to favorable selection. Although previous research found no difference in self-reported health for Kaiser Permanente members compared with individuals from northern California with other forms of private insurance (indemnity plans, preferred provider plans, or Medicare supplemental plan),<sup>8</sup> our membership may be somewhat healthier than the general population. Kaiser Permanente members younger than 65 years are primarily employed and thus typically healthy enough to work. However, it is difficult to conceive that such a selection

process would act differentially across ethnic groups and complications.

### Limitations and Strengths

Hospital records are subject to misclassification, although previous medical record review validations suggested a high level of reliability. Additionally, regional comparisons are limited because Latinos in northern California are almost exclusively Mexican American, whereas Latinos from the East Coast are more typically of Cuban or Puerto Rican ethnic origin. Our Asian membership is ethnically heterogeneous (eg, Chinese, Japanese, Korean, or Filipino), and pooled estimates may mask important variation. Another limitation is that we were unable to control for family size, so larger families would appear to have a higher risk of diabetes despite equal prevalence of diabetes. We were unable to establish with certainty that the access to or quality of health care received by the study cohort was equivalent across ethnic groups. However, previous and several current studies in this population have failed to detect substantive ethnic differences. No black-white differences were detected in a chart review study of 8 primary preventive care measures for diabetes.<sup>68</sup> Similarly, no substantive ethnic differences were detected in the use of angiotensin-converting enzyme inhibitors and angiotensin II AT-1 receptor antagonists.<sup>69</sup> A national study of the quality of health care among patients with diabetes<sup>70</sup> detected no substantive or significant differences in the rates of annual primary care visits and eye examinations across ethnic groups within Kaiser Permanente (A.J.K., unpublished data, 2000-2002). These findings were also confirmed by 2 internal Kaiser Permanente surveys that failed to detect important ethnic disparities in recommended processes of care for diabetic patients (A.J.K., unpublished data, 1994-1997, 2001).

The major strengths of this study are its inclusion of a wide range of complications, prospective design, large sample size with rich clinical and behavioral data, and generalizability to insured pa-

tients with diabetes. Our diabetes registry identifies patients who do not have pharmacotherapy prescriptions through laboratory findings and outpatient diagnosis, providing a more representative diabetic sample than pharmacy-based registries that fail to capture such patients or studies from diabetes specialty clinics that typically include patients with more severe disease.<sup>71</sup>

### CONCLUSIONS

Despite comparable health insurance coverage, ethnic disparities persist for each of the 5 major complications of diabetes. Ethnic disparities in this population were generally smaller than those reported in population-based studies. Ethnic patterns showed no consistency across complications. Surprisingly, a wide range of socioeconomic, behavioral, and clinical factors explained few of the observed ethnic disparities. Although they are evidence by default, the robust findings within ethnic groups along with the inconsistent patterns across ethnic groups are consistent with a genetic role in the etiology. Although minority risk of diabetic complications may be smaller than that of whites, minorities still bear a substantial burden because of complications, given their greatly increased prevalence of diabetes.<sup>72-75</sup>

This study facilitates a realistic assessment of the potential to meet national health objectives set by the Initiative to Eliminate Racial and Ethnic Disparities in Health, assuming additional steps are taken toward equalizing access and quality of care across ethnic groups. Although eliminating ethnic disparities in complications for patients with diabetes is certainly a worthwhile goal, it is currently unrealistic. Targets, if not ethnic specific, should be based on the lowest complication rates, which are more often experienced by minorities (eg, Asian LEA rates) rather than the white majority. To assess whether ethnic disparities can be eliminated and to design appropriate interventions, we need a better understanding of the extent to which disparities have a genetic basis and the

nature of their nongenetic causes. Although providing similar medical coverage alone will not eliminate disparities, equal access to quality care will probably confer the greatest reduction in ethnic disparities in diabetes-related complications.

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## REFERENCES

- US Department of Health and Human Services. President's Race and Health Disparities Initiative 2000. Available at: <http://www.omhrc.gov>. Accessibility verified March 20, 2002.
- Cowie CC, Port FK, Wolfe RA, Savage PJ, Moll PP, Hawthorne VM. Disparities in incidence of diabetic end-stage renal disease according to race and type of diabetes. *N Engl J Med*. 1989;321:1074-1079.
- Rostand SG, Kirk KA, Rutsky EA, Pate BA. Racial differences in the incidence of treatment for end-stage renal disease. *N Engl J Med*. 1982;306:1276-1279.
- Pugh JA, Stern MP, Haffner SM, Eifler CW, Zapata M. Excess incidence of treatment of end-stage renal disease in Mexican Americans. *Am J Epidemiol*. 1988;127:135-144.
- Lavery LA, Ashry HR, van Houtum W, Pugh JA, Harkless LB, Basu S. Variation in the incidence and proportion of diabetes-related amputations in minorities. *Diabetes Care*. 1996;19:48-52.
- Smedley BD, Stith AY, Nelson AR, eds. *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care*. Washington, DC: National Academy Press; 2002.
- Krieger N. Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology. *Am J Public Health*. 1992;82:703-710.
- Gordon NP, Kaplan GA. Some evidence refuting the HMO "favorable selection" hypothesis: the case of Kaiser Permanente. *Adv Health Econ Health Serv Res*. 1991;12:19-39.
- Hiatt RA, Friedman GD. Characteristics of patients referred for treatment of end-stage renal disease in a defined population. *Am J Public Health*. 1982;72:829-833.
- Ferrara A, Karter AJ, Ackerson LM, Liu JY, Selby JV. Hormone replacement therapy is associated with better glycemic control in women with type 2 diabetes: the Northern California Kaiser Permanente Diabetes Registry. *Diabetes Care*. 2001;24:1144-1150.
- Iribarren C, Karter AJ, Go AS, et al. Glycemic control and heart failure among adult patients with diabetes. *Circulation*. 2001;103:2668-2673.
- Karter AJ, Ackerson LM, Darbinian JA, et al. Self-monitoring of blood glucose levels and glycemic control: the Northern California Kaiser Permanente Diabetes Registry. *Am J Med*. 2001;111:1-9.
- Karter AJ, Ferrara A, Darbinian J, Ackerson LM, Selby JV. Self-monitoring of blood glucose: language and financial barriers in a managed care population with diabetes. *Diabetes Care*. 2000;23:477-483.
- Karter AJ, Newman B, Rowell S, et al. Large-scale collection of family history data and recruitment of informative families for genetic analysis. *J Registry Manage*. 1998;25:7-12.
- Karter AJ, Rowell SE, Ackerson LM, et al. Excess maternal transmission of type 2 diabetes: the Northern California Kaiser Permanente Diabetes registry. *Diabetes Care*. 1999;22:938-943.
- Selby JV. Linking automated databases for research in managed care settings. *Ann Intern Med*. 1997;127:719-724.
- Selby JV, Ettinger B, Swain B, Brown JB. First 20 months' experience with use of Metformin for type 2 diabetes in a large health maintenance organization. *Diabetes Care*. 1999;22:38-44.
- Selby JV, Ray GT, Zhang D, Colby CJ. Excess costs of medical care for patients with diabetes in a managed care population. *Diabetes Care*. 1997;20:1396-1402.
- Selby JV, Karter AJ, Ackerson LM, Ferrara A, Liu J. Developing a prediction rule from automated clinical databases to identify high-risk patients in a large population with diabetes. *Diabetes Care*. 2001;24:1547-1555.
- International Classification of Diseases, Ninth Revision, Clinical Modification*. Washington, DC: Public Health Service, US Dept of Health and Human Services; 1988.
- Arellano MG, Petersen GR, Petitti DB, Smith RE. The California Automated Mortality Linkage System (CAMLIS). *Am J Public Health*. 1984;74:1324-1330.
- McKee PA, Castelli WP, McNamara PM, Kannel WB. The natural history of congestive heart failure: the Framingham Study. *N Engl J Med*. 1971;285:1441-1446.
- Selby JV, Zhang D. Risk factors for lower extremity amputation in persons with diabetes. *Diabetes Care*. 1995;18:509-516.
- Pi-Sunyer XF, et al. *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report*. Bethesda, Md: National Institutes of Health, National Heart, Lung, and Blood Institute; 1998.
- Adler AI, Boyko EJ, Ahroni JH, Stensel V, Forsberg RC, Smith DG. Risk factors for diabetic peripheral sensory neuropathy: results of the Seattle Prospective Diabetic Foot Study. *Diabetes Care*. 1997;20:1162-1167.
- Christen WG, Manson JE, Bubes V, Glynn RJ, for the Sorbinil Retinopathy Trial Research Group. Risk factors for progression of distal symmetric polyneuropathy in type 1 diabetes mellitus. *Am J Epidemiol*. 1999;150:1142-1151.
- Reiber GE, Pecoraro RE, Koepsell TD. Risk factors for amputation in patients with diabetes mellitus: a case-control study. *Ann Intern Med*. 1992;117:97-105.
- Diabetes Surveillance, 1997*. Atlanta, Ga: Centers for Disease Control and Prevention; 1997.
- DeStefano F, Newman J. Comparison of coronary heart disease mortality risk between black and white people with diabetes. *Ethn Dis*. 1993;3:145-151.
- Stern MP, Haffner SM. Type II diabetes and its complications in Mexican Americans. *Diabetes Metab Rev*. 1990;6:29-45.
- Haffner SM, Mitchell BD, Stern MP, Hazuda HP. Macrovascular complications in Mexican Americans with type II diabetes. *Diabetes Care*. 1991;14:665-671.
- Revers M, Shetterly SM, Baxter J, Marshall JA, Hamman RF. Prevalence of coronary heart disease in subjects with normal and impaired glucose tolerance and non-insulin-dependent diabetes mellitus in a bi-ethnic Colorado population: the San Luis Valley Diabetes Study. *Am J Epidemiol*. 1992;135:1321-1330.
- Leggetter S, Chaturvedi N, Filler JH, Edmonds ME. Ethnicity and risk of diabetes-related lower extremity amputation: a population-based case-control study of African Caribbeans and Europeans in the United Kingdom. *Arch Intern Med*. 2002;162:73-78.
- Most RS, Sinnock P. The epidemiology of lower extremity amputations in diabetic individuals. *Diabetes Care*. 1983;6:87-91.
- Miller AD, Van Buskirk A, Verhoek-Oftedahl W, Miller ER. Diabetes-related lower extremity amputations in New Jersey, 1979 to 1981. *J Med Soc N J*. 1985;82:723-726.
- Gujral JS, McNally PG, O'Malley BP, Burden AC. Ethnic differences in the incidence of lower extremity amputation secondary to diabetes mellitus. *Diabet Med*. 1993;10:271-274.
- Incidence of treatment for end-stage renal disease attributed to diabetes mellitus, by race/ethnicity—Colorado, 1982-1989. *MMWR Morb Mortal Wkly Rep*. 1992;41:845-848.
- Pugh JA, Medina RA, Cornell JC, Basu S. NIDDM is the major cause of diabetic end-stage renal disease: more evidence from a tri-ethnic community. *Diabetes*. 1995;44:1375-1380.
- Burden AC, McNally PG, Feehally J, Walls J. Increased incidence of end-stage renal failure secondary to diabetes mellitus in Asian ethnic groups in the United Kingdom. *Diabet Med*. 1992;9:641-645.
- Schneider EC, Zaslavsky AM, Epstein AM. Racial disparities in the quality of care for enrollees in Medicare managed care. *JAMA*. 2002;287:1288-1294.
- Mayberry RM, Mili F, Ofili E. Racial and ethnic differences in access to medical care. *Med Care Res Rev*. 2000;57(suppl 1):108-145.
- Pugh JA, Tuley MR, Hazuda HP, Stern MP. The influence of outpatient insurance coverage on the microvascular complications of non-insulin-dependent diabetes in Mexican Americans. *J Diabetes Complications*. 1992;6:236-241.
- Harris MI. Racial and ethnic differences in health insurance coverage for adults with diabetes. *Diabetes Care*. 1999;22:1679-1682.
- Wagstaff A, van Doorslaer E. Income inequality and health: what does the literature tell us? *Annu Rev Public Health*. 2000;21:543-567.
- Backlund E, Sorlie PD, Johnson NJ. A comparison of the relationships of education and income with mortality: the National Longitudinal Mortality Study. *Soc Sci Med*. 1999;49:1373-1384.
- Lantz PM, House JS, Lepkowski JM, Williams DR, Mero RP, Chen J. Socioeconomic factors, health behaviors, and mortality: results from a nationally representative prospective study of US adults. *JAMA*. 1998;279:1703-1708.
- Robbins JM, Vaccarino V, Zhang H, Kasl SV. Excess type 2 diabetes in African-American women and men aged 40-74 and socioeconomic status: evidence from the Third National Health and Nutrition Examination Survey. *J Epidemiol Community Health*. 2000;54:839-845.
- Burge MR, Lucero S, Rassam AG, Schade DS. What are the barriers to medical care for patients with newly diagnosed diabetes mellitus? *Diabetes Obes Metab*. 2000;2:351-354.
- Reese S, Owen P, Bender B, Potts G, et al. Levels of diabetes-related preventive-care practices: United States, 1997-1999. *MMWR Morb Mortal Wkly Rep*. 2000;49:954-958.
- Freeman HP, Payne R. Racial injustice in health care. *N Engl J Med*. 2000;342:1045-1047.
- Kahn KL, Pearson ML, Harrison ER, et al. Health care for black and poor hospitalized Medicare patients. *JAMA*. 1994;271:1169-1174.
- Ayanian JZ. Race, class, and the quality of medical care. *JAMA*. 1994;271:1207-1208.
- Conigliaro J, Whittle J, Good CB, et al. Under-

- standing racial variation in the use of coronary revascularization procedures: the role of clinical factors. *Arch Intern Med.* 2000;160:1329-1335.
54. Ayanian JZ, Cleary PD, Weissman JS, Epstein AM. The effect of patients' preferences on racial differences in access to renal transplantation. *N Engl J Med.* 1999;341:1661-1669.
55. Chaturvedi N, Stephenson JM, Fuller JH. The relationship between socioeconomic status and diabetes control and complications in the EURODIAB IDDM Complications Study. *Diabetes Care.* 1996;19:423-430.
56. Connolly VM, Kesson CM. Socioeconomic status and clustering of cardiovascular disease risk factors in diabetic patients. *Diabetes Care.* 1996;19:419-422.
57. Chaturvedi N, Jarrett J, Shipley MJ, Fuller JH. Socioeconomic gradient in morbidity and mortality in people with diabetes: cohort study findings from the Whitehall Study and the WHO Multinational Study of Vascular Disease in Diabetes. *BMJ.* 1998;316:100-105.
58. Adler NE, Newman K. Socioeconomic disparities in health: pathways and policies. *Health Aff (Millwood).* 2002;21:60-76.
59. Soumerai SB, Ross-Degnan D, Avorn J, McLaughlin T, Choodnovskiy I. Effects of Medicaid drug-payment limits on admission to hospitals and nursing homes. *N Engl J Med.* 1991;325:1072-1077.
60. Williams MV, Parker RM, Baker DW, et al. Inadequate functional health literacy among patients at two public hospitals. *JAMA.* 1995;274:1677-1682.
61. Gornick ME, Eggers PW, Reilly TW, et al. Effects of race and income on mortality and use of services among Medicare beneficiaries. *N Engl J Med.* 1996;335:791-799.
62. van Ryn M, Burke J. The effect of patient race and socio-economic status on physicians' perceptions of patients. *Soc Sci Med.* 2000;50:813-828.
63. Krieger N, Sidney S, Coakley E. Racial discrimination and skin color in the CARDIA study: implications for public health research. *Am J Public Health.* 1998;88:1308-1313.
64. Schneeweiss S, Maclure M, Walker AM, Grottendorst P, Soumerai SB. On the evaluation of drug benefits policy changes with longitudinal claims data: the policy maker's versus the clinician's perspective. *Health Policy.* 2001;55:97-109.
65. Ferguson R, Grim CE, Opgenorth TJ. A familial risk of chronic renal failure among blacks on dialysis? *J Clin Epidemiol.* 1988;41:1189-1196.
66. Freedman BI, Tuttle AB, Spray BJ. Familial predisposition to nephropathy in African-Americans with non-insulin-dependent diabetes mellitus. *Am J Kidney Dis.* 1995;25:710-713.
67. Risch N, Burchard E, Zid E, Tang H. Categorizations of humans in biomedical research: genes, race, and disease. *Genome Biol.* In press.
68. Martin TL, Selby JV, Zhang D. Physician and patient prevention practices in NIDDM in a large urban managed-care organization. *Diabetes Care.* 1995;18:1124-1132.
69. Rosen AB, Karter AJ, Schneider EC, Liu JY, Selby JV. Lack of racial and ethnic disparities in ACE-inhibitor use among patients with diabetes. Paper presented at: Society for General Internal Medicine; May 2-4, 2002; Atlanta, Ga.
70. The Translating Research Into Action for Diabetes (TRIAD) Study: a multicenter study of diabetes in managed care. *Diabetes Care.* 2002;25:386-389.
71. Bruno G, Cavallo-Perin P, Barger G, et al. Cardiovascular risk profile of type 2 diabetic patients cared for by general practitioners or at a diabetes clinic: a population-based study. *J Clin Epidemiol.* 1999;52:413-417.
72. Mokdad AH, Ford ES, Bowman BA, et al. Diabetes trends in the US: 1990-1998. *Diabetes Care.* 2000;23:1278-1283.
73. Harris MI, Flegal KM, Cowie CC, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in US adults: the Third National Health and Nutrition Examination Survey, 1988-1994. *Diabetes Care.* 1998;21:518-524.
74. Sloan NR. Ethnic distribution of diabetes mellitus in Hawaii. *JAMA.* 1963;183:419-424.
75. *Diabetes in America.* Bethesda, Md: National Diabetes Data Group, National Institute of Diabetes and Digestive and Kidney Diseases; 1995.

Nothing contributes so much to tranquilize the mind  
as a steady purpose—a point on which the soul may  
fix its intellectual eye.

—Mary Wollstonecraft Shelley (1797-1851)