A Community-Based Study of Explanatory Factors for the Excess Risk for Early Renal Function Decline in Blacks vs Whites With Diabetes

The Atherosclerosis Risk in Communities Study

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Context: The explanation for the excess risk for diabetic renal disease in blacks is uncertain.

Objectives: To compare the incidence of early renal function decline in black and white adults with diabetes and to examine possible explanatory factors for racial differences.

Design: Prospective cohort study.

Setting: Four US communities participating in the Atherosclerosis Risk in Communities study.

Participants: Community-based sample of 1434 diabetic adults aged 45 to 64 years.

Measurements: Detailed baseline assessment using structured interview, results of physical examination, and laboratory measurements.

Main Outcome: Development of early renal function decline defined by an increase in serum creatinine of at least 35.4 µmol/L (0.4 mg/dL) during 3 years of follow-up.

Results: During 3 years of follow-up, early renal function decline developed in 45 blacks (28.4 per 1000 person-years [PY]) and 25 whites (9.6 per 1000 PY). After adjustment for age, sex, and baseline serum creatinine level, early renal function decline was more than 3 times as likely to develop in blacks than whites (odds ratio, 3.15; 95% confidence interval, 1.86-5.33). Additional adjustment for education, household income, health insurance, fasting glucose level, mean systolic blood pressure, smoking history, and physical activity level reduced the relative odds in blacks to 1.38 (95% confidence interval, 0.71-2.69), corresponding to an 82% reduction in excess risk.

Conclusions: These data suggest that early renal function decline is 3 times more likely to develop in blacks than whites and that potentially modifiable factors, including lower socioeconomic status, suboptimal health behaviors, and suboptimal control of glucose level and blood pressure, account for more than 80% of this disparity.

Arch Intern Med. 1999;159:1777-1783

Renal disease is responsible for significant morbidity and mortality among Americans with diabetes mellitus, and treatment costs alone result in an estimated annual expenditure of more than $2 billion. In fact, approximately 40% of all new cases of end-stage renal disease (ESRD) in the United States are due to diabetes, making it the leading cause of ESRD. Furthermore, the prevalence of ESRD among persons with diabetes has been increasing by approximately 16% annually since 1987, a rate surpassing any other cause of ESRD.

Although it is well established that blacks with diabetes have an approximately 2- to 3-fold higher risk for development of ESRD compared with whites, the explanation for this disparity is uncertain. Previous black-white comparisons of diabetic renal disease risk have had several limitations. Some have used suboptimal data on exposures to renal disease risk factors derived from claims data or retrospective surveys. Others have used suboptimal ecological study designs that substitute group data for information that is unavailable on the individual. Finally, some have been based on nonrepresentative samples such as clinic populations with limited generalizability.

Moreover, most of these studies focused exclusively on ESRD. Therefore, little is known about differences in the early natural history of renal disease between blacks and whites. In theory, the excess of ESRD among blacks could be due to an increased risk for progression to early renal function decline or to suboptimal medical management once renal insufficiency has developed. Both hypotheses have different implications.
SUBJECTS AND METHODS

SETTING

The Atherosclerosis Risk in Communities (ARIC) study is an on-going prospective study that examines risk factors for subclinical and clinical atherosclerotic disease in a cohort of 15,792 persons, aged 45 to 64 years at baseline. The participants were selected by probability sampling from the following 4 US communities: Forsyth County, North Carolina; Jackson, Miss; the northwest suburbs of Minneapolis, Minn; and Washington County, Maryland. More than 90% of black participants in the study are from Jackson. Sampling procedures and methods are described in detail elsewhere. Our analysis was based on 3 years of follow-up, which included a baseline visit from January 1, 1986, to December 31, 1989, and a follow-up clinic visit at year 3 (1990-1992).

PARTICIPANTS

At baseline, 1886 ARIC participants had diabetes mellitus as defined by the presence of any of the following criteria: use of oral hypoglycemic medication or insulin, self-reported physician diagnosis, fasting serum glucose level of at least 7.0 mmol/L (126 mg/dL), or nonfasting glucose level of at least 11.1 mmol/L (200 mg/dL). We excluded participants who reported ethnicity other than black or white (n = 3), who had baseline creatinine level of at least 176.8 µmol/L (2.0 mg/dL) (n = 27), had missing exposure data (n = 149), died before the year 3 visit (n = 116), were unavailable for follow-up (n = 149), or were missing data on serum creatinine level at the year 3 visit (n = 8). After these exclusions, 1434 participants remained. Compared with their counterparts with complete data, participants who were unavailable for follow-up or had missing data were more likely to be black (68.7% vs 30.3%), to lack insurance coverage (27.1% vs 16.3%), to have household incomes of less than $16,000 per year (53.8% vs 30.2%), and to have not completed a high school education (45.3% vs 36.9%) (all P<.001). There were no significant differences with regard to age, sex, fasting serum glucose level, mean systolic blood pressure, smoking history, leisure physical activity level, baseline serum creatinine level, or serum creatinine level change during 3 years of follow-up.

EXPOSURE ASSESSMENT

Baseline examination included interviews in the home and clinic, physical examinations, and laboratory measurements. Participants fasted at least 12 hours before the blood draw. Blood was drawn from the antecubital vein while the participants were seated. Anticoagulant-free vacutainer tubes were used. All blood analyses were performed at the central chemistry laboratory at University of Minnesota, Minneapolis. Serum glucose level was assessed using a modified hexokinase–glucose-6-phosphate dehydrogenase procedure, a glucose reference method of the Centers for Disease Control and Prevention, Atlanta, Ga. Information on race, sex, age, education, household income, presence of health insurance, history of hypertension, medication use, and smoking history was obtained from the home and clinic interviews conducted at the baseline visit. Height and weight were measured while participants were not wearing shoes. Body mass index at baseline was defined as the weight in kilograms divided by the square of the height in meters. Physical activity was assessed by interview based on a modification of the questionnaire developed by Baecke et al. The results from the questionnaire were condensed into a continuous leisure-related physical activity index of 1 to 5, with 1 indicating the lowest level of activity and 5, the highest level. Blood pressure was measured using a random-0 sphygmonometer while the participant was seated and had no change in posture for 5 minutes. The mean of the second and third of 3 blood pressure measurements was used for our analyses.

OUTCOME ASSESSMENT

The primary outcome was early renal function decline, defined as a 35.4-µmol/L (0.4-mg/dL) increase in serum creatinine level from baseline to year 3. At baseline and year 3, creatinine level was measured using a modified

for developing the most effective strategy to prevent ESRD in this population.

We therefore conducted a prospective cohort study to examine factors associated with black-white differences in early renal function decline in a biracial, community-based cohort of middle-aged adults with diabetes. We were particularly interested in whether differences in established and suspected risk factors for diabetic nephropathy (eg, blood pressure and glycemic control, access to health care, and health behaviors) could explain differences in renal disease risk between blacks and whites.

RESULTS

BASELINE CHARACTERISTICS

Table 1 shows the baseline characteristics of the participants by race. Compared with their white counterparts, blacks were younger, more likely to be female, less likely to have completed high school, more likely to have an annual household income below $16,000, more likely to smoke, and less likely to have health insurance. In addition, blacks had higher average systolic blood pressure, fasting serum glucose level, and body mass index, but a lower leisure-related physical activity index. Duration of diabetes was similar in the 328 blacks and 547 whites who provided this information (7.4 vs 7.0 years, respectively; P=.48). There was also no difference in mean serum creatinine levels (97.2 vs 97.2 µmol/L [1.1 vs 1.1 mg/dL], respectively; P=.13) or use of angiotensin-converting enzyme inhibitors between blacks and whites at baseline.

EARLY RENAL FUNCTION DECLINE AT YEAR 3

By year 3, mean serum creatinine levels were higher among blacks than whites (108.7 vs 101.7 µmol/L [1.23

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kinetic Jaffe method.\textsuperscript{22} Within the ARIC study, the short-term, day-to-day, within-person variability for creatinine level is 4.3\%, and the methodological variance is 4.6\%. The minimal detectable change (\(\Delta\)) at which one can be 95\% confident that a subsequent creatinine value represents a true change from a baseline measurement is given using the following equation:

\[
\Delta = 2.77 \left( \sigma_{wp}^2 + \sigma_{w}^2 \right)^{1/2},
\]

where \(\sigma_{wp}\) is within person variance, and \(\sigma_{w}\) is variance due to the procedure for measuring serum creatinine level.\textsuperscript{21} Thus, in the ARIC study, the minimal detectable difference at which one can be 95\% confident that the degree of change in creatinine value represents a true difference is 15.9 µmol/L (0.2 mg/dL).\textsuperscript{22} We examined changes that were twice this size, or at least 35.4 µmol/L (0.4 mg/dL) as markers of renal function decline.

### Statistical Analysis

Initially, baseline characteristics of blacks and whites were compared using \(t\) tests for continuous variables and \(\chi^2\) tests for categorical variables. Next, we calculated incidence rates using the person-years (PY) approach and calculated 95\% confidence intervals (CIs) using the method described by Kahn and Sempos.\textsuperscript{21} Bivariate analyses were then performed to evaluate the association of each baseline variable with early renal function decline. Baseline variables were grouped as follows: (1) health behaviors, including smoking status (current, former, or never) and leisure-related physical activity; (2) physiological variables, including fasting serum glucose level and systolic blood pressure; and (3) socioeconomic variables, including level of highest education achieved, annual household income, and possession of health insurance. Finally, we constructed a series of 5 logistic regression models to determine the relative odds (RO) of renal function decline in blacks vs whites after adjustment for the following: (1) age, sex, and baseline serum creatinine level; (2) age, sex, baseline serum creatinine level, and health behaviors; (3) age, sex, baseline serum creatinine level, and physiological variables; (4) age, sex, baseline creatinine level, and socioeconomic variables; and (5) all of the above variables simultaneously. The percent excess risk (PER) explained by a set of risk factors was calculated using the following formula:

\[
\text{PER} = \frac{P_B - P_W}{P_B - 1},
\]

where \(P_B\) is the RO of early renal function decline in blacks vs whites adjusted only for age, sex, and baseline serum creatinine level, and \(P_W\) is the RO adjusted for age, sex, baseline serum creatinine level, and the above-listed variable sets.\textsuperscript{21} This formula is an adaptation from the original, which is based on relative risks; however, ROs approximate relative risks when the outcome is uncommon (ie, affects <10\% of the cohort, as in our study). The PER is calculated as a fraction of the partially adjusted excess risk (risk above and beyond the risk in whites, or a relative risk of 1). Thus, if the RO in blacks vs whites were 3.0, and adjustment for a set of variables were found to reduce this RO to 2.0, it would explain \((3 − 2)/(3 − 1) = 50\%\) of the excess risk in blacks compared with whites.

Interactions between risk variables for blacks and whites were also tested, and no statistically significant differences were found (data not shown). All statistical analyses were performed using commercially available software (SAS statistical package; SAS Institute, Cary, NC).

### Subsidiary Analyses

To determine the robustness of the main analysis, we conducted a series of subsidiary analyses. The first analysis used a different measure of renal function decline, a 25\% decline in estimated creatinine clearance from baseline defined by the Cockcroft-Gault formula.\textsuperscript{24} The second analysis was performed after excluding participants with type 1 diabetes mellitus. To construct this subgroup, we removed participants who received a diagnosis of diabetes at 30 years or younger and who were taking insulin at the baseline visit (\(n = 80\)). A third analysis was performed using only participants with complete data on duration of diabetes obtained from questionnaires administered at the year 6 visit (\(n = 875\)). Finally, analyses were performed with continuous outcome variables for change in creatinine level from baseline and change in estimated creatinine clearance using linear regression.

### Predictors of Early Renal Function Decline

Unadjusted associations between baseline characteristics and the development of early renal function decline are shown in Table 3. Blacks were approximately 3 times more likely to have development of early renal function decline than their white counterparts. In addition, baseline serum creatinine level, systolic blood pressure, and serum glucose level were positively associated with the risk for early renal function decline. In contrast, greater educational attainment, possession of health insurance, annual household income of $16 000 or more, and higher leisure physical activity were associated with a lower rate of early renal function decline. Age, sex, body mass index, use of angiotensin-converting enzyme inhibitors, and smoking history were not associated with incident early renal function decline in this cohort.

### Excess Risk of Early Renal Function Decline in Blacks vs Whites

Table 4 shows the ROs of early renal function decline in blacks vs whites with sequential adjustment for groups of potential explanatory factors. Body mass index and use of angiotensin-converting enzyme inhibitors were not included in the multivariate models because they were not associated with early renal function decline in the unadjusted analysis. The baseline model was adjusted for...
age, sex, and serum creatinine level at baseline. Adjusting for these variables, early renal function decline was more than 3 times as likely to develop in blacks than in their white counterparts (RO, 3.15; 95% CI, 1.86-5.33). Additional adjustment for health behaviors, including smoking history and leisure-related physical activity level, reduced the RO to 2.82, corresponding to a 15% reduction in the excess risk for development of early renal function decline in blacks. Addition of physiological variables, including systolic blood pressure and fasting glucose level, to the base model attenuated the RO substantially, reducing the excess risk by 49%. Addition of socioeconomic characteristics, including presence of health insurance, education, and annual household income, to the base model reduced the RO to 2.03, corresponding to a 52% reduction in excess risk. Finally, simultaneous adjustment for age, sex, serum creatinine levels, health behaviors, and socioeconomic and physiologic variables produced an 82% reduction in the excess risk for early renal function decline among blacks and reduced the RO to a level that was no longer statistically significant (RO, 1.38; 95% CI, 0.71-2.69).

To better understand the contribution of specific variables within each group, we conducted separate analyses that adjusted for age, sex, baseline creatinine level, and each variable separately. We found that income and education each explained 6% of the excess risk for development of early renal function decline in blacks compared with whites. Leisure-related physical activity and systolic blood pressure each explained 18%, whereas glucose level alone explained 32% of the excess risk. In contrast, insurance status and smoking history did not explain any of the excess risk for early renal function decline among blacks.

### SUBSIDIAL ANALYSES

To determine the robustness of the results, we also analyzed the data using an alternate definition of early renal function decline, at least a 25% decrease in creatinine clearance calculated using the Cockcroft-Gault method. Using this alternate outcome, there were 69 incident cases during 3 years of follow-up. Of those, 40 participants were black (25.2 per 1000 PY) and 29 were white (11.1 per 1000 PY). There was 84% agreement between individuals defined as having early renal function decline by this alternate definition and those defined by the development of a change in creatinine level of at least 35.4 µmol/L (0.4 mg/dL). Furthermore, this alternate definition led to similar results. After adjustment for age, sex, and creatinine level at baseline, the RO of developing at least a 25% reduction in creatinine clearance was more than 2-fold higher in blacks than whites (RO, 2.42; 95% CI, 1.45-4.03). Additional adjustment for smoking history and leisure physical activity level had almost no effect on the odds ratio (RO, 2.34; 95% CI, 1.36-4.02). However, adjustment for socioeconomic variables reduced the RO substantially (RO, 1.65; 95% CI, 0.93-2.95), corresponding to a 54% reduction in excess risk. Adjustment for systolic blood pressure and mean fasting glucose level led to a comparable reduction in the excess risk (RO, 1.73; 95% CI, 1.01-2.96; 49% reduction in excess risk). Finally, simultaneous adjustment for age, sex, serum creatinine level, health behaviors, and physiological and socioeconomic

### Table 1. Selected Baseline Characteristics of 1434 Diabetic Adults Aged 45 to 64 Years by Race

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Whites (n = 885)</th>
<th>Blacks (n = 549)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean ± SD, y</td>
<td>56.0 ± 5.6</td>
<td>55.0 ± 5.7</td>
<td>.001</td>
</tr>
<tr>
<td>Female, %</td>
<td>47.5</td>
<td>66.3</td>
<td>.001</td>
</tr>
<tr>
<td>Socioeconomic, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education*</td>
<td>Less than high school</td>
<td>8.7</td>
<td>26.4</td>
</tr>
<tr>
<td></td>
<td>High school or vocational school</td>
<td>45.9</td>
<td>28.4</td>
</tr>
<tr>
<td></td>
<td>College or professional school</td>
<td>29.7</td>
<td>22.0</td>
</tr>
<tr>
<td>Health insurance</td>
<td>93.0</td>
<td>75.2</td>
<td>.001</td>
</tr>
<tr>
<td>Household income, $*</td>
<td>&lt;16 000</td>
<td>11.9</td>
<td>52.1</td>
</tr>
<tr>
<td></td>
<td>16 000-34 999</td>
<td>38.4</td>
<td>24.4</td>
</tr>
<tr>
<td></td>
<td>≥35 000</td>
<td>41.4</td>
<td>11.1</td>
</tr>
<tr>
<td>Physiologic, mean ± SD</td>
<td>Systolic blood pressure, mm Hg</td>
<td>127 ± 18</td>
<td>132 ± 22</td>
</tr>
<tr>
<td></td>
<td>Fasting glucose, mmol/L (mg/dL)</td>
<td>9.5 ± 3.8</td>
<td>11.0 ± 5.0</td>
</tr>
<tr>
<td></td>
<td>(171 ± 68)</td>
<td>(199 ± 90)</td>
<td></td>
</tr>
<tr>
<td>Health behaviors</td>
<td>Physical activity index, mean ± SD†</td>
<td>2.4 ± 0.5</td>
<td>2.0 ± 0.6</td>
</tr>
<tr>
<td>Smoking, %</td>
<td>Current</td>
<td>20.7</td>
<td>22.8</td>
</tr>
<tr>
<td></td>
<td>Former</td>
<td>37.6</td>
<td>25.3</td>
</tr>
<tr>
<td></td>
<td>Never</td>
<td>41.7</td>
<td>51.9</td>
</tr>
<tr>
<td>Other</td>
<td>Serum creatinine, µmol/L (mg/dL)</td>
<td>97.2 (1.1)</td>
<td>97.2 (1.1)</td>
</tr>
<tr>
<td>Diabetes duration, mean ± SD‡</td>
<td>7.0 ± 8.7</td>
<td>7.4 ± 9.0</td>
<td>.48</td>
</tr>
<tr>
<td>Body mass index, mean ± SD</td>
<td>30.4 ± 5.7</td>
<td>32.0 ± 5.9</td>
<td>.001</td>
</tr>
<tr>
<td>Use of angiotensin-converting enzyme inhibitors, %</td>
<td>5.6</td>
<td>5.9</td>
<td>.80</td>
</tr>
</tbody>
</table>

* Percentages do not total 100%, because not all respondents answered this question.
† Explained in the “Exposure Assessment” subsection of the “Subjects and Methods” section.
‡ Based on 875 individuals who provided this information at the year 6 visit.

### Table 2. Incidence of Early Renal Function Decline in 1434 ARIC Participants With Diabetes, by Race*

<table>
<thead>
<tr>
<th>Participants</th>
<th>No. of Persons at Risk at Baseline</th>
<th>Person-Years of Follow-up</th>
<th>No. of Persons Affected</th>
<th>Incidence per 1000 Person-Years</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blacks</td>
<td>549</td>
<td>1587</td>
<td>45</td>
<td>28.4</td>
<td>20.4-36.4</td>
</tr>
<tr>
<td>Whites</td>
<td>885</td>
<td>2601</td>
<td>25</td>
<td>9.6</td>
<td>5.9-13.3</td>
</tr>
</tbody>
</table>

*ARIC indicates Atherosclerosis Risk in Communities study.
Simultaneous adjustment for age, sex, baseline creatinine level, and duration of diabetes, early renal function decline was 3.1 times as likely to develop in blacks as in whites (RO, 2.82; 95% CI, 1.61-4.93; Reference: 1.49-6.53). Simultaneous adjustment for age, sex, baseline creatinine level, duration of diabetes, health behaviors, and socioeconomic and physiological variables resulted in a 66% decline in the excess risk for development of early renal function decline in blacks.

Finally, we analyzed our results using continuous rather than dichotomous measures of early renal function decline, and the results were substantially unchanged. Adjustment for age, sex, creatinine level at baseline, health behaviors, and socioeconomic and physiological variables resulted in a 100% reduction in the progression of serum creatinine levels among blacks and a 66% reduction in the progression of declining creatinine clearance.

These data support 2 main conclusions. First, early renal function decline is 3 times more likely to develop in blacks with diabetes mellitus than in whites. Second, potentially modifiable factors, such as lower socioeconomic status, suboptimal health behaviors, and suboptimal control of glucose level and blood pressure, largely account for this disparity. Our study has several strengths, including its community-based sample, its prospective design, and its consistent results using several different definitions of early renal function decline. In particular, this is one of the few studies of black-white differences in renal disease with individual-level data on key physiological risk factors such as blood pressure and glucose level.

Nonetheless, several potential limitations of the study deserve comment. First, the study lacked data on microalbuminuria, a sensitive marker of early diabetic nephropathy. Since creatinine level change is a less sensitive marker, we likely misclassified some individuals with early diabetic nephropathy as “normal.” Nevertheless, this definition is highly specific and represents a slightly later point in the natural history of diabetic renal disease. Furthermore, without data on microalbuminuria, it is likely that some instances of renal function decline in our study...
were related to factors other than diabetic nephropathy (eg, hypertension, nephrotoxins). However, there are methodological advantages to lumping various types of renal pathology into a single outcome category, since renal disease in diabetes is often multifactorial, and since the classification of specific renal abnormalities without biopsy evidence is not definitive.²⁷

Second, the use of change in creatinine level as a measure of early renal function decline lacks the precision of sequentially measured glomerular filtration rate as a means of monitoring renal function. Nevertheless, the Modification of Diet and Renal Disease study identified a strong correlation ($r = 0.73$) between this measure and directly measured glomerular filtration rate for more than 1 year of follow-up.²⁸ Moreover, most previous prospective studies on the risk factors for progression of renal disease have used serum creatinine level as an outcome.²⁹⁻³¹ In addition, our results were remarkably similar using several different definitions of early renal function decline.

Third, since most of the black participants were from a single site (Jackson), we cannot exclude the possibility that geographic variation might have confounded our results. However, previous studies show little geographic variation in incidence rates of ESRD in the 4 states that serve as the setting for the ARIC study. (In 1992, ESRD incidence rates adjusted for age, sex, and race per million population were 166 in Maryland, 150 in Minnesota, 161 in Mississippi, and 168 in North Carolina.)³²

Fourth, information on age at onset and duration of diabetes was unavailable for 39.4% of the participants. Lack of information on duration makes distinction between types 1 and 2 diabetes mellitus impossible. Nevertheless, there is general consensus that the pathophysiological basis and risk factors for diabetic nephropathy are similar in both forms of diabetes.³³ Furthermore, subsidiary analysis restricted to individuals with type 2 diabetes mellitus suggests that these results are at least applicable to type 2 diabetes.

A final limitation of the study was the lack of data on glycohemoglobin, which is a more accurate measure of long-term glycemic control than is fasting serum glucose level. Nevertheless, fasting glucose levels were strongly associated with risk for early renal function decline in our study and have been found to correlate very well with overall glycemic control among individuals with type 2 diabetes mellitus who comprised most of our sample.³⁴ Furthermore, random misclassification related to imprecise characterization of glycemic control would likely have introduced a conservative bias toward the null.

Since 1973, there have been 11 studies looking at black-white differences in the progression to diabetes-related ESRD.⁴⁻¹³,¹⁶ All have documented excess risk for blacks vs whites (median relative risk in blacks vs whites, 3.4; range, 2.6⁻5.3). Of these, only 4 studies had data on potential explanatory factors.¹¹⁻¹³,¹⁶ Two of the studies examining the explanatory factors associated with black-white differences in the progression to ESRD were limited by a lack of individual-level data on renal disease risk factors.¹¹,¹³ Byrne et al¹³ looked at the impact of socioeconomic status on the incidence of ESRD related to diabetes using race-specific median family income by ZIP code. They found a positive correlation between incidence of ESRD and declining income in whites, but no significant relationship in blacks. Nevertheless, they lacked information on clinical risk factors or health behaviors. Brancati and colleagues¹¹ used statewide survey data to control for black-white differences in the prevalence of hypertension, diabetes, cigarette smoking, and poorly controlled hypertension, as well as completion of college education, income of at least $10,000, presence of health insurance, and presence of regular source of medical care using population level data derived from ZIP codes. Based on their analyses, those authors were unable to explain the increased incidence of ESRD in blacks based on a higher prevalence of known risk factors. However, compared with studies of individuals, ecological studies like these are especially susceptible to confounding and misclassification.

In a retrospective, clinic-based study of patients with diabetes and hypertension, Tierney et al¹² found that an increased incidence of early renal function decline (serum creatinine level ≥176.8 µmol/L [2.0 mg/dL]) among blacks persisted despite adjustment for differences in blood pressure and glucose level control between blacks and whites.¹² This clinic-based study, however, was limited by its use of nonstandardized measures of blood pressure as well as the fact that its subjects were selected from an urban university clinic and were therefore not representative of the general population. Perrigae et al¹⁰ combined data from an ESRD registry with survey information from patients. Their analysis only captured information on socioeconomic variables, including income level, presence and type of health insurance, and number of missing teeth. Adjustment for these factors partially explained the increased odds of ESRD in blacks with diabetes. Thus, none of these studies were fully able to explain the black-white disparity in diabetic renal disease. Nevertheless, all were limited by their inability to evaluate simultaneously the potential impact of racial differences in sociodemographic characteristics, physiologic measurements, and health-related behaviors on the incidence of ESRD.

Because of US history, race is a complex variable, standing not only for ancestry, but also for an array of environmental, behavioral, and sociocultural factors.³⁵⁻³⁷ Our analysis suggests that such nonheritable, potentially modifiable factors account for much of the excess risk for renal disease in blacks. Whether the remaining excess risk for renal disease in blacks left unexplained in the multivariate model is related to residual confounding due to inadequate precision in the measurement of renal disease risk factors or to differences in variables not included in our analysis is outside the scope of our study.

Our study has 2 possible implications. First, it suggests that major differences in renal function decline between blacks and whites occur early in the natural history of renal disease. This represents a point in the natural history where individuals are likely to be under the care of primary care physicians or endocrinologists, rather than nephrologists. Second, most of the excess risk for renal disease in blacks appears to be due to potentially modi-
fiable factors such as control of blood pressure and glyce-
mia and to socioeconomic markers related to access to
health care. Thus, our results suggest that interventions
to reduce black-white disparities in renal disease
should be aimed at improving health care for blacks early
in the course of their diabetes.

Accepted for publication December 1, 1998.

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Public Health, Minneapolis (Dr Shahar); and the Depart-
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cal Center, Jackson (Dr Watson).

This study was supported in part by the Robert Wood
Johnson Clinical Scholars Program, Princeton, NJ (Dr Krop);
grant DK48362 from the National Institute of Diabetes and
Digestive and Kidney Disease and GCRC grants RR007722
and RR0035 from the National Center for Research Re-
sources, Bethesda, Md (Dr Coresh); and a Clinical Re-
search Award from the American Diabetes Association, Al-
exandria, Va (Dr Brancati). The ARIC study is performed
as a collaborative study supported by the National Heart,
Lung, and Blood Institute (Bethesda, Md) contracts N01-
HC-55015, N01-HC-55016, N01-HC-55018, N01-HC-
55019, N01-HC-55020, N01-HC-55021, and N01-HC-
55022.

Reprints: Frederick L. Brancati, MD, MHS, 2024 E
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REFERENCES

tion 95-1468.

eseases; 1997.

3. Rodby RA. Type II diabetic nephropathy: its clinical course and therapeutic im-

4. Easterling RE. Racial factors in the incidence and causation of end-stage renal

5. Rostand SG, Kirk KA, Rutsky EA, Pate BA. Racial differences in the incidence of

6. Eggers PW, Connorton R, McMullan M. The Medicare experience with end-
stage renal disease: trend in incidence, prevalence, and survival. Health Care Fi-

7. Weller JM, Wu SH, Furguson GW, Hawthorne VM. End-stage renal disease in
Michigan: incidence, underlying causes, prevalence, and modalities of treat-

8. 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 dia-

9. Ferguson R, Grun CE. Oppegnor T.J. The epidemiology of end-stage renal dis-
Health. 1987;77:864-865.

10. Stephens GW, Gillaspay JA, Clyne D, Mejia A, Pollak VE. Racial differences in
the incidence of end-stage renal disease in type I and II diabetes mellitus. Am J Kid-

of diabetic end-stage renal disease among blacks: a population-based study of

12. Tierney WM, McDonald CJ, Luft FC. Renal disease in hypertensive adults: effect

13. Byrne C, Nadelman J, Luke RG. Race, socioeconomic status, and the develop-

14. Lopes AS, Port FK. Differences in the patterns of age-specific black/white com-
parisons between end-stage renal disease attributable and not attributed to dia-

15. Lopes AA, Port FK, James SA, Agodoa L. The excess risk of treated end-stage
1971.

16. Pernecky TV, Whelton PK, Klag MJ. Race and end-stage renal disease: socio-
economic status and access to health care as mediating factors. Arch Intern Med.

17. The ARIC Investigators. The Atherosclerosis Risk in Communities (ARIC) Study:

18. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Re-
port of the Expert Committee on the Diagnosis and Classification of Diabetes Mel-

19. Basinke JA, Burema J, Fritters JE. A short questionnaire for the measurement of ha-

20. National Heart, Lung and Blood Institute Atherosclerosis Risk in Communities

21. Harris EC, Yassaka T. On the calculation of a “reference change” for comparing

22. Eckfeldt JH, Chambless LE, Shen YL. Short-term, within-person variability in clini-


24. Breslow NE, Day NE. Statistical Methods in Cancer Research. Lyon, France: In-
ternational Agency for Research on Cancer, IARC Publications; 1990:76-78. Pub-
lication 32.

25. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creati-

26. Mogensen CE, Christensen JK, Vittinghus E. The stages in diabetic renal dis-
ease with emphasis on the stage of incipient diabetic nephropathy. Diabetes. 1993;
32:64-78.

27. Pernecky TV, Brancati FL, Whelton PK, Klag MJ. Studying the causes of kidney
disease in humans: a review of methodologic obstacles and possible solutions.

28. Modification of Diet in Renal Disease (MDRD) Study Group. Assessing the pro-
gression of renal disease in clinical studies: effect of duration of follow-up and

29. Schulman NB, Ford CE, Hall WD. Prognostic value of serum creatinine and ef-
fect of treatment of hypertension on renal function: results from the Hyperten-
sion Detection and Follow-up Program: the Hypertension Detection and Fol-

30. Walker WG, Neaton JD, Cutler JA, Neuvirth R, Cohen JD, for the MRFFIT Re-
search Group. Renal function change in hypertensive members of the Multiple Risk Factor Intervention Trial: racial and treatment effects. JAMA. 1992;268:
3059-3061.

31. Pernecky TV, Nieto FJ, Whelton PK, Klag MJ, Comstock GW, Szlko M. A pro-
spective study of blood pressure and serum creatinine: results from the “CLUE” Study and the ARIC Study. JAMA. 1993;269:488-493.

Institutes of Health, National Institute of Diabetes and Digestive and Kidney Dis-
eases; September 1992.


34. Brustman L, Langer O, Engel S, Anyaegbunam A, Mazze R. Verified self-
monitored blood glucose data versus glycosylated hemoglobin and glyco-
sylated serum protein as a means of predicting short- and long-term metabolic

35. Pernecky TV, Klag MJ, Whelton PK. Race and socioeconomic status in hyper-

36. Muntaner C, Nieto FJ, O’Campo P. The Bell Curve: on race, social class, and epi-

37. Navarro V. Race or class versus race and class: mortality differentials in the United