



## Invited Commentary

### Invited Commentary: Untangling the Web of Diabetes Causality in African Americans

Richard W. Grant<sup>1,2</sup>

<sup>1</sup> Division of General Medicine, Massachusetts General Hospital, Boston, MA.

<sup>2</sup> Harvard Medical School, Boston, MA.

Received for publication March 23, 2007; accepted for publication April 4, 2007.

Diabetes is more prevalent and its consequences more severe in African Americans than in Whites. Efforts to understand and eliminate the root causes of disparities in the prediabetic state offer the potential to reduce the tremendous “downstream” costs of diabetes for patients and society. The accompanying study by Schootman et al. (*Am J Epidemiol* 2007;166:379–387) presents provocative new data on the apparently significant role of an individual’s own housing condition in the odds of subsequent diabetes development. Despite methodological limitations in measurement and adjustment for confounding, this paper offers new insights into potential mediators of diabetes development. Efforts to effectively address the problem of disparities in the prediabetic state will require greater interdisciplinary collaboration between unfamiliar disciplines and wider implementation of the randomized clinical trial design.

African Americans; diabetes mellitus; genetics; housing; prediabetic state; questionnaires; residence characteristics

African Americans have a higher prevalence of diabetes (1), poorer control of diabetes-related risk factors (2, 3), and a greater burden of diabetes-related complications compared with Whites (4, 5). Efforts to reduce disparities in this population have been expensive (6) and have had limited success (7, 8). A recent finding that African Americans continuously enrolled in a high-quality health maintenance organization had higher hemoglobin A1c levels at time of first diagnosis underscores the concept that disparities in disease progression begin even prior to diagnosis and treatment (9). Moreover, African Americans tend to have higher blood pressure at time of initial diabetes diagnosis compared with their White counterparts (10), placing them at an early increased risk of cardiovascular complications, the leading cause of death in diabetes (11).

Given that the disparities in disease severity between African Americans and other US racial/ethnic groups begin early and worsen over time (12), it is imperative to search for the fundamental cause of these differences during the

prediabetic period. Focusing attention on the “root sources” of racial/ethnic differences in the prediabetic state offers the potential to better understand the social, individual, and physiologic factors driving health disparities; ideally, such understanding would provide a blueprint for interventions that effectively eliminate disparities before they inflict their full burden on our patients and society (13).

The paper by Schootman et al. (14) in this issue of the *Journal* provides provocative new data on predictors of incident diabetes among African Americans. The authors used prospective cohort data from the African-American Health Study to examine the association of both neighborhood and individual housing conditions with subsequent diabetes incidence among 644 African-American subjects without diabetes at baseline. After 3 years of follow-up, the condition of the respondents’ houses at baseline (cleanliness, physical condition of the building’s interior and exterior, and condition of the furnishings as rated by the interviewers) was strongly predictive of new diabetes, whereas conditions

of the neighborhood and block face were not. Unadjusted odds ratios for these housing condition associations ranged from 1.8 to 2.5.

No one believes that the status of one's home is a *causative* factor in the development of diabetes (putting aside the very unlikely potential role of toxins, which—as the authors point out (14)—would be expected to be a neighborhood-level rather than individual-home-level factor). Rather, the condition of an individual's home appears to serve as a marker for some important underlying factor(s). Two possibilities that come immediately to mind are that poor housing conditions may be a much more sensitive measure of relative poverty; alternatively, perhaps the status of one's home is correlated with health-related behaviors (exercise, eating patterns) that influence subsequent risk of diabetes.

Given the strength of the signal transmitted by individual housing conditions in this study (14), the key next step is to more clearly understand the underlying causal agent(s) driving this association with subsequent diabetes diagnosis. To further explore these associations, the authors presented four mutually exclusive “mediating pathways” for diabetes development (health behaviors, psychosocial factors, health status, and medical care access) and found that including the variables from each of these pathways had minimal impact on the crude odds ratios for the primary exposure of housing conditions, leading them to conclude that “housing conditions may produce the observed effect by another untested pathway” (14, p. 385).

Two critical shortcomings of this “mediating pathway” approach are 1) the limited capacity of the chosen variables to fully capture a given pathway, and 2) the inability to accurately model the temporal and combined interactions between pathways. These limitations undermine the measurement precision of the proposed mediating pathways. For example, the “health behavior” pathway included the Yale Physical Activity Index and smoking, but not medication adherence or diet (a critical factor in diabetes development). Similarly, the “psychosocial” pathway included social support (from the Medical Outcomes Study) and depression (Center for Epidemiologic Studies Depression Scale), but not health-related motivation or desire to avoid complications of diabetes. Complicating matters further, the “health behavior” pathway could be a consequence of the “psychosocial” pathway, or vice versa. Similar arguments can be made for insufficient measurement of “health status” (e.g., body mass index, diagnosis of hypertension, and several other factors, but not insulin resistance or types and doses of medications used) and “access” (e.g., insurance status and ability to see a physician in the prior year, but not measures of patient-physician trust or continuity of care). Clearly, health care access will influence one's subsequent health status, and both of these pathways are intimately related to both health behavior and psychosocial status.

To address concerns about their mediating pathways, the authors (14) used propensity scores to integrate all potential mediators into a single predictive model; this strategy also had limited impact on the calculated odds ratios. This finding is not too surprising given the measurement limitations of potential confounders. For example, exercise should be measured over a long period of time (rather than a cross-

sectional association between health status and the past 7 days of exercise) to avoid the problem of reverse causation whereby people who are obese or in poor health are less likely to exercise. Moreover, the study was conducted in two neighborhoods (inner-city and suburban) in and around St. Louis, Missouri. The somewhat restricted variability in neighborhoods (and, by extension, the health behaviors that tend to cluster by neighborhood) tends to emphasize the predictive value of the more variable housing condition results within neighborhoods.

How should we interpret the impact of individual housing conditions on incident diabetes from these adjusted analyses? Known predictors of diabetes include family history, higher body mass index, and risk factor clustering (the so-called metabolic syndrome) (10, 15–17). Family history presumably reflects both genetic risks and the gene-environment interactions that determine disease expression. These environmental factors (ranging from prenatal and childhood weight to adult exercise and smoking behavior) influence adult body weight, physical fitness, and “endothelial health” (18). An intriguing implication of the Schootman et al. paper (14) is that there may be a family-level “subculture”—how one family cooks, shops, and feels about his or her personal health—in addition to the higher-order environmental factors captured by local neighborhood, economic stratum, or racial designation. Because this study was conducted among African Americans only, we have no way of knowing the relative effect of housing conditions in other race/ethnic groups.

In the United States, race is a complex marker for socio-cultural and historical factors with limited genetic validity (19, 20). Studies focused specifically on racial differences in diabetes onset tend to fall into the distinct disciplines of genetics, physiology, health services research, and environmental/public health. Genetics effects are small, are difficult to justify in the context of US “racial” categories, and are influenced by gene-environmental interactions. These environmental influences include the social and cultural behaviors that may lead to weight gain or detrimental food choices, which in turn modify the (genetically determined) physiology. The local and society-level effects of racism, poverty, and quality of care add another layer of mediators to more proximal “causative” factors. Efforts to move this field forward will require greater interdisciplinary collaboration and exchange of ideas between researchers from very different backgrounds: geneticists with social epidemiologists, physiologists with health services researchers, economists with nutritionists.

Successful strategies to address the fundamental causes of disparities in the prediabetic state have the potential to markedly reduce or eliminate the severe “downstream” complications of diabetes. In attempting to parse confounding, colinearity, and causality in observational studies of incipient diabetes, it becomes clear that nothing is clear (21). In the hierarchy of clinical study designs, observational studies such as this one (14) are well suited for generating hypotheses; we now need an increased commitment to randomized trials for nonconfounded tests of hypotheses directed at eliminating disparities in the prediabetic state. For example, if we hypothesize from Schootman et al.'s data

that family-level health behaviors are the confounder linking housing condition to future diabetes risk, a reasonable next step could be to implement a home-based randomized intervention that directly addresses family health-related attitudes in high-risk homes.

## ACKNOWLEDGMENTS

Dr. Grant is supported by a Career Development Award (NIDDK K23 DK067452) from the National Institute of Diabetes and Digestive and Kidney Diseases.

Conflict of interest: none declared.

## REFERENCES

- Harris MI, Flegal KM, Cowie CC, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988–1994. *Diabetes Care* 1998;21:518–24.
- Kirk JK, D'Agostino RB Jr, Bell RA, et al. Disparities in HbA1c levels between African-American and non-Hispanic white adults with diabetes: a meta-analysis. *Diabetes Care* 2006;29:2130–6.
- Harris M, Eastman R, Cowie C, et al. Racial and ethnic differences in glycemic control of adults with type 2 diabetes. *Diabetes Care* 1999;22:403–8.
- Lanting LC, Joung IMA, Mackenbach JP, et al. Ethnic differences in mortality, end-stage complications, and quality of care among diabetic patients: a review. *Diabetes Care* 2005;28:2280–8.
- Wong MD, Shapiro MF, Boscardin WJ, et al. Contribution of major diseases to disparities in mortality. *N Engl J Med* 2002;347:1585–92.
- Glazier RH, Bajcar J, Kennie NR, et al. A systematic review of interventions to improve diabetes care in socially disadvantaged populations. *Diabetes Care* 2006;29:1675–88.
- el-Kebbi IM, Ziemer DC, Musey VC, et al. Diabetes in urban African-Americans. IX. Provider adherence to management protocols. *Diabetes Care* 1997;20:698–703.
- Sequist TD, Adams A, Zhang F, et al. Effect of quality improvement on racial disparities in diabetes care. *Arch Intern Med* 2006;166:675–81.
- Adams AS, Zhang F, Mah C, et al. Race differences in long-term diabetes management in an HMO. *Diabetes Care* 2005;28:2844–9.
- Brancati FL, Kao WHL, Folsom AR, et al. Incident type 2 diabetes mellitus in African American and white adults: the Atherosclerosis Risk in Communities Study. *JAMA* 2000;283:2253–9.
- Hu FB, Stampfer MJ, Haffner SM, et al. Elevated risk of cardiovascular disease prior to clinical diagnosis of type 2 diabetes. *Diabetes Care* 2002;25:1129–34.
- Karter AJ, Ferrara A, Liu JY, et al. Ethnic disparities in diabetic complications in an insured population. *JAMA* 2002;287:2519–27.
- Link BG, Phelan J. Understanding sociodemographic differences in health—the role of fundamental social causes. *Am J Public Health* 1996;86:471–3.
- Schootman M, Andresen EM, Wolinsky FD, et al. The effect of adverse housing and neighborhood conditions on the development of diabetes mellitus among middle-aged African Americans. *Am J Epidemiol* 2007;166:379–87.
- Hariri S, Yoon PW, Moonesinghe R, et al. Evaluation of family history as a risk factor and screening tool for detecting undiagnosed diabetes in a nationally representative survey population. *Genet Med* 2006;9:752–9.
- Shai I, Jiang R, Manson JE, et al. Ethnicity, obesity, and risk of type 2 diabetes in women: a 20-year follow-up study. *Diabetes Care* 2006;29:1585–90.
- Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. *Diabetes Care* 2005;28:1769–78.
- Olden K, White SL. Health-related disparities: influence of environmental factors. *Med Clin North Am* 2005;89:721–38.
- Karter AJ. Race and ethnicity: vital constructs for diabetes research. *Diabetes Care* 2003;26:2189–93.
- Barr DA. The practitioner's dilemma: can we use a patient's race to predict genetics, ancestry, and the expected outcomes of treatment? *Ann Intern Med* 2005;143:809–15.
- Krieger N. Epidemiology and the web of causation: has anyone seen the spider? *Soc Sci Med* 1994;39:887–903.