**ARIC Manuscript Proposal # 960**

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| **PC Reviewed: 09/10/03** | **Status: A** | **Priority: 2** |
| **SC Reviewed: 09/11/03** | **Status: A** | **Priority: 2** |

**1.a. Full Title**:

Individual and area-level life-course SES and decline in renal function: the Atherosclerosis Risk in Communities Study

**b. Abbreviated Title (Length 26 characters)**:

SES trajectory and CRI

**2. Writing Group (list individual with lead responsibility first)**:

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**3. Timeline**:

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| October, 2003 | Obtain ARIC data; begin analysis |
| August, 2004 | First draft of results |
| December, 2004 | Submit manuscript(s) for ARIC approval |

**4. Rationale**:

Kidney disease prevalence and incidence rates show an inverse social gradient that is typical of many chronic conditions.

This social gradient is most striking in the comparison of white and African-American rates: African-Americans have over four times the incidence rate as whites (USRDS, 2002; Matins et al., 2002). The gradient by race-ethnicity has also been observed for serum creatinine, a marker of subclinical renal insufficiency, using NHANES data (Coresh et al., 2001). Racial differences in incidence appear to be primarily the result of socioeconomic status differentials, as evidenced by attenuation of relative kidney disease risk when individual education and household income (Krop et al., 1999) and contextual median income (Klag et al, 1997) are held constant. Although the focus of this paper will not be on race *per se*, it is recognized as an important form of social stratification with health consequences. Much of the social epidemiology of renal disease has focused on this topic.

Multiple factors mediate the relationship between socio-economic status (SES) and disease (Link and Phelan, 1995), and kidney disease is no exception. Hypertension and diabetes are the underlying cause in over 70% of incident cases of kidney disease. Other identified factors for kidney damage include smoking (Hogan, 2001), access to health care (Perneger et al, 1995), HIV infection (Szczech, 2001), alcohol and illicit drug use (Crowe et al., 2000), heavy metal exposure to cadmium, lead, and mercury (ATSDR, 1999a-c; Wedeen, 1997), high-protein diet (Dwyer et al., 1994), and plasma lipids (Muntner, 2000).

Most work relating individual-level socioeconomic position to overall and cause-specific mortality has used cross-sectional or prospective cohort designs, relating current SES to current or prospective health conditions. Under such a model, SES is considered a static category; education level is the favored measure, due in part to its stability after early adulthood (Lynch and Kaplan, 2000).

The life course model has been employed for several decades in sociology, psychology, and human development (Featherman, 1985), and is now being incorporated into research on health outcomes. The life course model of SES has been proposed as a more robust alternative to static definitions of SES (Kuh et al., 1997; Davey Smith et al., 1998).

Although individuals have a life-course SES trajectory, this trajectory occurs within a dynamic context. The socio-economic characteristics of a neighborhood may change due to out-migration of wealthy residents (Wilson, 1987), to generalized changes in social and economic structure (Blau and Duncan, 1967), or to some combination of factors such as availability of jobs and racial segregation (Massey and Gross, 1994; Quillian, 1999). These changes are differential by SES and race, and they impact health (Krieger, 2000). However, life course exposure to different neighborhood conditions has not been examined in relation to renal disease.

**5. Main Hypothesis/Study Questions**:

The primary hypothesis is: low individual SES across the life course is associated with risk of kidney disease.

Three theories of individual life course SES will be used:

- A "cumulative" model, which views low SES as an insult which accumulates over the life course; a score of cumulative disadvantage is the exposure of interest
- A "trajectory" model, which regards social mobility as the salient SES characteristic

- A "categorical" model, which treats each stage of the life course (childhood, young adulthood, middle age, and retirement) as an independent exposure. The latency model (Barker, 1992) is one example of a categorical model.

The second hypothesis is that contextual SES at birth and across the life course is both an independent risk factor and effect modifier of the relationship between individual-level SES measures and kidney disease. For example, individuals born to low-SES parents who spent childhood in a disadvantaged neighborhood are hypothesized to be at increased risk of kidney disease; on the other hand, growing up in a wealthy neighborhood may mitigate some of the effect associated with childhood disadvantage.

A secondary analysis will assess which biological and social attributes mediate the relationship between SES and kidney disease. Mediators will be investigated by adjusting for the mediators in adulthood. For example, if the childhood SES-kidney disease association is attenuated upon adjustment for hypertension, this will be evidence in favor of hypertension as a mediator of this relationship.

**6. Data (variables, time window, source, inclusions/exclusions)**:

Outcome variable

Decreased kidney function is the outcome variable. Kidney function will be assessed in three ways:

1. according to National Kidney Foundation (2002) K/DOQI guidelines for stage 3 or higher kidney disease (GFR < 60)
2. an increase in serum creatinine of 0.4 mg/dL at visits 2 or 4 (Krop et al., 1999; Muntner, 2000)
3. diagnosis of a kidney disease (such as ESRD)

GFR will be estimated using the modified MDRD formula (Levey et al., 1999). These three outcomes will be used in combination to define "kidney disease." Annual change in GFR will be assessed by subtracting the latest visit GFR from the baseline GFR in the follow-up visits, and dividing by the number of years in between.

Main exposure variables

- Context during childhood, at ages 30, 40, and 50 years will be defined using the Life-course SES Ancillary Study of ARIC. Context at time of inclusion into ARIC will be defined by place of residence at that time.
- Contextual SES will be assessed during childhood, at ages 30, 40, and 50 years, and at the time of induction into ARIC. Contextual SES will be defined using census data, at the level of county for 1930 and 1940 observations, and at the level of census tract for later censuses. As the available data changes across censuses, a robust measure of contextual SES will be chosen.
- Individual SES will be assessed in several manners:
  (1) by parental education (for childhood)
  (2) by highest education level (at time of ARIC)

(3) by level of control at work, for parent (childhood SES) and self, at 30, 40, and 50 years old, and at time of inclusion in ARIC
(4) by parental (childhood) and self's occupational status at ages 30, 40, and 50, and at the time of inclusion in ARIC.

- Contextual trajectories will be defined by moving up or down in relative contextual SES rank, from childhood, and at each point along the life course at which data was collected (ages 30, 40, 50, and at time of ARIC). A measure that allows comparability across censuses for each point in the life course will be used.
- Individual trajectories will be defined categorically as:
  (1) Having higher, lower, or same level of education as one's parents
  (2) Having a greater, lesser, or same degree of control at work as in previous points in the life course
  (3) Having higher, lower, or same occupation ranking

Covariates

- Due to the difficulty of separating social and other aspects of race (Kaufman et al., 1997), race will be addressed through stratification. Age and gender will be treated as covariates.
- A secondary analysis will investigate the role of mediating factors such as diabetes mellitus, hypertension, and access to health care.

**Statistical methods**

A mixed model will be employed that simultaneously adjusts for individual and contextual SES across the life-course, taking into account the SES of a neighborhood at the time the ARIC participant lived there. Clustering will be by census tract. As just one outcome measure (low GFR at any visit, or change in GFR over all ARIC visits) will be used, there is no clustering of observations within individuals.

**7.a. Will the data be used for non-CVD analysis in this manuscript? _X_ Yes ____ No**

**b. If Yes, is the author aware that the file ICTDER02 must be used to exclude persons with a value RES_OTH = "CVD Research" for non-DNA analysis, and for DNA analysis RES_DNA = "CVD Research" would be used? _X_ Yes ____ No**
(This file ICTDER02 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

**8.a. Will the DNA data be used in this manuscript? ____ Yes _X_ No**

**8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER02 must be used to exclude those with value RES_DNA = "No use/storage DNA"? ____ Yes ____ No**

**9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status.**

ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://bios.unc.edu/units/cscc/ARIC/stdy/studymem.html

___X__ Yes _____ No

**10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?**

Proposal # 836 (Lead author: Sharon Merkin): A longitudinal analysis of area and individual socioeconomic status, race, and early renal impairment: The Atherosclerosis Risk in Communities Study.

The author has been contacted and has stated no overlap exists between studies.

**11. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.**

References


Agency for Toxic Substances and Disease Registry (ATSDR). 1999a. Toxicological profile for cadmium. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

Agency for Toxic Substances and Disease Registry (ATSDR), 1999b. Toxicological profile for lead. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

Agency for Toxic Substances and Disease Registry (ATSDR). 1999c. Toxicological profile for mercury. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

Barker, DJP, 1992. Fetal and Infant Origins of Adult Diseases. London: BMJ Press.

Blau, Peter M. and Dudley Duncan, 1967. *The American Occupational Structure*. New York: Free Press.

Coresh, JC, GL Wei, G McQuillan, et al., 2001. Prevalence of high blood pressure and elevated serum creatinine levels in the United States. *Archives of Internal Medicine* 161:1207-1216.

Crowe, AV, M Howse, GM Bell, and JA Henry, 2000. Substance abuse and the kidney (review). QJM 93:147-152.

Davey Smith, G, C Hart, D Blane, and D Hole, 1998. Adverse socioeconomic conditions in childhood and cause specific adult mortality: prospective occupational study. BMJ 316:1631-35.

Diez-Roux, A, 1998. Bringing context back into epidemiology: Variables and fallacies in multilevel analysis. AJPH 88:216-22.

Dwyer, JT, JH Madans, B Turnbull, et al., 1994. Diet, indicators of kidney disease, and later mortality among older persons in the NHANES I Epidemiologic Follow-up Study. AJPH 84:1299-1303.

Featherman, DL and RM Lerner, 1985. Ontogenesis and sociogenesis: problematics for theory and research about development and socialization across the lifespan. *American Sociological Review* 50:659-76.

Hogan, SL, 2001. The association of cigarette smoking and kidney function. Doctoral dissertation: University of North Carolina at Chapel Hill Department of Epidemiology.

Kaufman, J, R Cooper, and D McGee, 1997. Socioeconomic status and health in blacks and whites: the problem of residual confounding and the resiliency of race." Epidemiology 8:621-8.

Klag, MJ, PK Whelton, BL Randall, et al., 1997. End-stage renal disease in African-American and white men: 16-year MRFIT findings. *JAMA* 277:1293-9.

Krieger, N, 2000. Discrimination and health. In *Social Epidemiology*, ed. by L Berman and I Kawachi. New York: Oxford University Press, pp.36-75.

Krop, JS, J Coresh, LE Chambless, et al., 1999. A community-based study of explanatory factors for the excess risk of early renal function decline in Blacks vs. Whites with diabetes: the Atherosclerosis Risk in Communities Study. *Archives of Internal Medicine* 159:1777-83.

Kuh, D, C Power, D Blane, and M Bartley, 1997. Social pathways between childhood and adult health. In *A life course approach to chronic disease epidemiology*, ed. by D Kuh and Y Ben-Schlomo. Oxford: Oxford University Press.

Levey, AS, JP Bosch, JB Lewis, et al., 1999. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. *Annals of Internal Medicine* 130:461-70.

Link, BG and J Phelan, 1995. Social Conditions as Fundamental Causes of Disease. *Journal of Health and Social Behavior* 35(S): 80-94.

Lynch, J and G Kaplan, 2000. Socioeconomic position. In *Social Epidemiology*, ed. by LF Berkman and I Kawachi. New York: Oxford University Press.

Martins, D, N Tareen, and KC Norris, 2002. The epidemiology of end-stage renal disease among African Americans. *American Journal of the Medical Sciences*. 323:65-11.

Massey, DS, and AB Gross, 1994. Migration, segregation, and the geographic concentration of poverty. *Annual Review of Sociology*, 59:425-45.

Muntner, P, J Coresh, JC Smith, et al., 2000. Plasma lipids and the risk of developing renal dysfunction: the Atherosclerosis Risk in Communities study. *Kidney International*, 58:293-301.

National Kidney Foundation (NKF), 2002. Kidney Disease Outcomes Quality Initiative (K/DOQI) Guidelines. Website at http://www.kidney.org/professionals/doqi/kdoqi, accessed on 4/20/03.

Perneger TV, PK Whelton, MJ Klag, 1995. Race and end-stage renal disease: socioeconomic status and access to health care as mediating factors. Arch Intern Med 155:1201-1208.

Quillian, L, 1999. Migration Patterns and the Growth of High-Poverty Neighborhoods, 1970-1990. *American Journal of Sociology*, 105(1):1-37.

Szczech, LA, 2001. Renal diseases associated with human immunodeficiency virus infection: epidemiology, clinical course, and management. Clinical Infectious Diseases 33:115-119.

USRDS, 2002: United States Renal Data System. *2002 Annual Data Report*. http://www.usrds.org/atlas.htm, accessed 2/2/03.

Wedeen, RP, 1997. Occupational and environmental renal disease. Seminars in Nephrology 17:46-53.

Wilson, WJ, 1987. *The truly disadvantaged*. Chicago: University of Chicago Press.