**ARIC Manuscript Proposal # 836**

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| **PC Reviewed: 10/16/01** | **Status: __A_** | **Priority: ___2_** |
| **SC Reviewed: 10/17/01** | **Status: __A_** | **Priority: ___2__** |

**1.a. Full Title:**

A longitudinal analysis of area and individual socioeconomic status, race, and early renal impairment: The Atherosclerosis Risk in Communities Study.

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

SES, race and renal impairment.

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

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*Including any interested ARIC investigators.

**3. Timeline:**

- Obtain data and initiate analyses: 11/01
- Initial results and first draft: 7/02
- Send to ARIC Publication Committee: 10/02

**4. Rationale:**

The association between socioeconomic status (SES) and end-stage renal disease (ESRD) incidence and mortality has been examined at both the individual (1-3) and area levels (4-10); most of these studies confirmed an inverse relationship between SES and ESRD incidence (1-6,8). Although some of this research sought to explain racial disparities in ESRD (1,2,5), many studies concluded that SES accounted for only some of the racial differences (1,3-5).

Much of the literature focuses on ESRD, with few studies investigating milder renal disease and SES (11,12). While a precursor to ESRD, renal function decline is also an independent risk factor for cardiovascular disease (13,14) and cerebrovascular (15) disease. Aside from the public health importance of preventing those diseases, the association between renal function decline and SES may shed new light on the racial disparities observed with regard to renal disease.

This proposal intends to examine area and individual-level socioeconomic indicators. Individual-level SES has been the focus of much of the epidemiologic literature regarding health and SES. SES information at the aggregate level, however, can reveal important elements of society that might be affecting one's health regardless of individual status (16-28). The effects of individual and area-level socioeconomic indicators on ESRD incidence have been shown in previous studies (1,4-7), and thus may be related to milder forms of renal insufficiency; to our knowledge, area-level SES and renal impairment has not yet been studied. Moreover, the independent effects of individual and area-level SES (examining each level while adjusting for the other) on ESRD or renal impairment have not yet been explored and may tease out the important SES elements in this relationship. Potential area-level indicators include: higher exposure to occupational or environmental nephrotoxins, (1,4) higher intake of over-the-counter analgesics, over-crowding, exposure to lead paint and Hantavirus organisms, higher prevalence of behaviors such as street drug use, and exposure to HIV,(1) less usage of Medicare coverage,(29) under-utilization of health care services, (1) and inaccessibility to health care (4,7) Other specific area-level factors not specific to renal disease may include exposure to crime and stress.(24,30)

Finally, this longitudinal study of renal impairment, as measured by estimated glomerular filtration rate (GFR), while accounting for changes in area-level SES and individual-level income at later visits, will examine the temporal relationship between SES and renal disease. That is, do people with renal function decline subsequently have lower incomes or move to lower SES areas, or do these socioeconomic changes precede renal impairment?

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

*Hypothesis*

Area-level and individual-level socioeconomic indicators are independently associated with renal function decline. Moreover, area and individual socioeconomic differences may explain racial disparities in renal disease incidence.

*Study Questions*

a) To examine the longitudinal association between renal function decline and individual and area-level socioeconomic status.

b) To specifically address the issue of racial differences with regard to renal impairment and assess this relationship after adjusting for area and individual-level socioeconomic status, as well as other relevant individual-level risk factors.

This proposal is part of a project to investigate renal impairment and SES in middle aged adults and adults aged 65 and older. Thus, we are interested in studying ARIC participants as well as the Cardiovascular Health Study (CHS) participants, adults aged 65 and older.

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

Variables: Serum creatinine, race, age, gender, prevalence of diabetes, systolic blood pressure, body-mass index, smoking, income, education, occupation, residential county, census tract and block group.

Time window: All visits, from visit 1: 1986-1989, to visit 4: 1996-1999.

Source:

- Baseline self-reported questionnaire: race, age, gender, smoking, income (this information was updated at visit 3), education occupation, residential information (this information was updated at visit 3).
- Clinical examination and blood analyses at baseline and follow-up: serum creatinine, systolic blood pressure, diabetes, body-mass index.
- 1990 Census data: neighborhood-level SES indicators.

Inclusions/exclusions: Include all participants with properly geocoded information on residential county, census tract and block group. Participants missing information on serum creatinine, race, age, gender or individual-level SES at intermediate visits will be excluded.

*Analysis*

Study population and variables of interest:

The outcome of interest in this study is renal function, as measured by estimated GFR at each visit. GFR is considered the best index of renal health and morbidity (31). Considering the clinical difficulty in measuring GFR, many researchers have used serum creatinine or creatinine clearance as estimates of GFR (11,12,32-36). These measurements, however, have been shown to be inaccurate in certain populations and in certain conditions (37,38) and thus may produce biased results. To overcome these limitations, GFR can be estimated by use of equations that take into account additional variables. The most popular of these, the Cockroft-Gault equation, considers weight, age, gender and serum creatinine to measure creatinine clearance (39). Recently a new prediction equation for GFR has been developed in conjunction with the Modification of Diet in Renal Disease (MDRD) Study that consists of serum creatinine, age, gender and race (40,41). These equations were tested using a gold standard measurement of GFR, and the MDRD equation provided more accurate and precise results (40). We will use this equation in the proposed study to estimate GFR, and thus examine renal function in this population. We will also conduct confirmatory analyses using the Cockroft-Gault equation to measure creatinine clearance and examining serum creatinine directly because of limitations in measuring the outcome, and in order to better explore racial differences.

GFR and its decline will primarily be examined as a dichotomous variable. A value of GFR<60 $ml/min/1.73m^2$ at any follow-up visit will be considered incidence of moderate chronic kidney disease as defined by the Chronic Kidney Disease Evaluation, Classification and Stratification Clinical Practice Guidelines Draft Document (41). An additional binary variable will be used, to define a decrease in GFR as incidence of renal function decline. Previous work

has shown that a decline in GFR of %30 or greater or a rise in creatinine of 0.4 mg/dl, reflect a clinically meaningful decline in kidney function (11,12,42). Utilizing follow-up hospitalization and medical records, we will also include as an event any participant who initiates dialysis or whose GFR<15 *ml/min/1.73m*$^2$. Confirmatory analyses will include examining estimated GFR and its decline as a continuous variable.

The independent variables of interest include:

1) Area-level SES indicators obtained from 1990 census linked by census tract at baseline, including income, education, occupation, poverty, housing and over-crowding. The SES indicators will be collapsed into categories based on the race-specific distributions as well as overall distributions.
2) Individual-level SES indicators include: income, education, and occupation.
3) Other individual-level risk factors known (and hypothesized) to be related to renal function decline will be examined and adjusted for, and include: race, gender, age, prevalence of diabetes, systolic blood pressure, BMI, smoking and baseline creatinine.
4) Additional variables will account for changes in residence (reflecting changes in SES) and changes in individual-level income, as these were updated at the third visit. Aside from adjusting for these changes, we will also examine them idependently in their association with renal impairment.

*Statistical analysis*

- Explore incidence of renal function decline (as defined above), measured at each and any visit, by race and gender. Incidence rates will be calculated using person years, based on individual follow-up dates. These rates will be adjusted for age and center using Poisson regression models. Incidence rates of moderate renal disease and more severe renal insufficiency will also be examined in this way.
- Relative hazard ratios by area indicators will be determined using discrete proportional hazards models. Area SES effects will be estimated before and after adjustment for individual-level SES indicators and other risk factors listed above.

Secondary analyses include:

- Repeat the models above examining creatinine clearance using the Cockroft-Gault equation. These models will consider a 0.4 mg/dl increase of creatinine as a measure of renal function decline, as consistent with other studies (11,12,42).
- Examine GFR as a continuous variable by individual and area-level SES indicators at each visit and by race and gender.
- Assess the longitudinal change of GFR by way of scatter plots and smoothing techniques.
- Construct generalized estimating equation (GEE) linear regression models (43) to estimate the mean changes of GFR over time and the effects of SES indicators, by pooling GFR values across visits and accounting for repeated individual measurements.

All these analyses will be stratified by race and gender (where appropriate). Multivariate models examining creatinine clearance will also be fit pooling race, in order to thoroughly examine racial

differences, as discussed in objective "b." Confirmatory analyses will include using SUDAAN to adjust for within neighborhood correlations (44). Moreover, additional variables will be included in the GEE models to account for any potential correlations within areas.

**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.**

___X___ Yes _____ No

**References:**


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

2. Whittle JC, Whelton PK, Seidler AJ, Klag MJ. Does racial variation in risk factors explain black-white differences in incidence of hypertensive end-stage renal disease? *Arch Intern Med* 1991:151:1359-1364.

3. Brancati FL, Whittle JC, Whelton PK, Seidler AJ, Klag MJ. The excess incidence of diabetic end-stage renal disease among blacks: a population based study of potential explanatory factors. *JAMA* 1992:268(21):3079-3084.

4. Young EW, Mauger EA, Jiang KH, Port FK, Wolfe RA. Socioeconomic status and end-stage renal disease in the United States. *Kidney International* 1994:45:907-911.

5. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Stamler J. End-stage renal disease in African-American and white men. *JAMA* 1997:277(16):1293-1298.

6. Rostand SG. US minority groups and end-stage renal disease: a disproportionate share. *American Journal of Kidney Diseases* 1992:14(5):411-413.

7. Byrne C, Nedelman J, Luke RG. Race, socioeconomic status, and the development of end-stage renal disease. *American Journal of Kidney Diseases* 1994:23(1):16-22.

8. Metcalfe W, MacLeod AM, Bennett D, Simpson K, Khan IH. Equity of renal replacement therapy utilization: a prospective population-based study. *QJM* 1999 Nov;92(11):637-42.

9. Port FK, Wolfe RA, Levin NW, Guire KE, Ferguson CW. Income and survival in chronic dialysis patients. *ASAIO Transactions* 1990:36:M154-M157.

10. Brancati FL, Whelton PK, Whittle JC, Klag MJ. Epidemiologic analysis of existing data to investigate hypertensive renal disease: an example from the Maryland End-Stage Renal Disease Registry. *American Journal of Kidney Diseases* 1993:21(4):Suppl 1:15-24.

11. Krop JS, Coresh J, Chambless LE, Shahar E, Watson RL, Szklo M, Brancati FL. 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. *Arch Intern Med* 1999:159;1777-1783.

12. Rostand SG, Brown G, Kirk KA, Rutsky RA, Dustan HP. Renal insufficiency in treated essential hypertension. *The New England Journal of Medicine* 1989:320;684-8.

13. Luft FC. Renal disease as a risk factor for cardiovascular disease. *Basic Res Cardiol* 2000;95(suppl 1):I72-I76.

14. Ruilope LM, Salvetti A, Jamerson K, Hansson L, Warnold I, Wedel H, Zancheti A. Renal function and intensive lowering of blood pressure in hypertensive participants of the Hypertension Optimal Treatment (HOT) Study. *J Am Soc Nephrol* 2001;12:218-225.

15. Wannamethee SG, Shaper AG, Perry IJ. Serum creatinine concentration and risk of cardiovascular disease: A possible marker for increased risk of stroke. *Stroke* 1997;28:557-563.

16. Andres TL, Baron AE, Wright RA, Marine WM. Tracking Community Sentinel Events: Breast Cancer Mortality and Neighborhood Risk for Advanced-Stage Tumors in Denver. *American Journal of Public Health* 1996;86(5):717-722.

17. Kaplan GA. People and Places: Contrasting Perspectives on the Association Between Social Class and Health. *International Journal of Health Services* 1996;26(3):507-519.

18. O'Campo P, Xue X, Wang MC, Caughy MO. Neighborhood Risk Factors for Low Birthweight in Baltimore: A Multilevel Analysis. *American Journal of Public Health* 1997;87(7):1113-1118.

19. Feinleib M. A New Twist in Ecological Studies. *American Journal of Public Health* 1998;88(10):1445-1446.

20. Diez-Roux AV. Bringing Context Back Into Epidemiology. *American Journal of Public Health* 1998;88(2):216-222.

21. Schwartz S. The Fallacy of the Ecological Fallacy: The Potential Misuse of a Concept and the Consequences. *American Journal of Public Health* 1994;84(5):819-824.

22. Susser M. The Logic in Ecological: I. The Logic of Analysis. *American Journal of Public Health* 1994;84(5):825-829.

23. Susser M. The Logic in Ecological: II. The Logic of Design. *American Journal of Public Health* 1994;84(5):830-835.

24. Jargowsky PA. *Poverty and Place: Ghettos, Barrios and the American City*. New York: Russel Sage Foundation; 1997.

25. Kaplan GA, Pamuk ER, Lynch JW, Cohen RD, Balfour JL. Inequality in Income and Mortality in the United States: Analysis of Mortality and Potential Pathways. *British Medical Journal* 1996;312(7037):999-1003.

26. Haan M, Kaplan GA, Camacho T. Poverty and Health: Prospective Evidence From the Alameda County Study. *American Journal of Epidemiology* 1987;125(6):989-998.

27. Haan MN, Kaplan GA, Syme SL. Socioeconomic Status and Health: Old Observations and New Thoughts. In: Bunker JP, Gomby DS, Kehrer BH, eds. *Pathways to Health: The Role of Social Factors*. Menlo Park, CA: The Henry J. Kaiser Foundation; 1989.

28. Wells BL, Horm JW. Targeting the Underserved for Breast and Cervical Cancer Screening: The Utility of Ecological Analysis Using the National Health Interview Survey. *American Journal of Public Health* 1998;88(10):1484-1489.

29. Gornick ME, Eggers PW, Reilly TW, Mentnech RM, Fitterman LK, Kucken LE, Vladeck BC. Effects of race and income on mortality and use of services among Medicare beneficiaries. *NEJM* 1996:335:791-9.

30. Link B, Phelan J. Social Conditions as Fundamental Causes of Disease. *Journal of Health and Social Behavior* 1995;(Extra Issue):80-94.

31. Levey AS. Measurement of renal function in chronic renal disease. *Kidney International* 1990;38:167-184.

32. Lindeman RD, Tobin J, Shock NW. Longitudinal studies on the rate of decline in renal function with age. *Journal of the American Geriatrics Society* 1985;33(4):278-285.

33. Coresh J, Toto RD, Kirk KA, Whelton PK, Massry S, Jones C, Agodoa L, Van Lente F, AASK Pilot Study Investigators. Creatinine clearance as a measure if GFR in screenees for the African-American Study of Kidney Disease and Hypertension Pilot Study. *American Journal of Kidney Diseases* 1998;32(1):32-42.

34. Coresh J, Wei L, McQuillan G, Brancati FL, Levey AS, Jones C, Klag MJ. Prevalence of high blood pressure and elevated serum creatinine level in the United States. *Arch Intern Med*. 2001;161:1207-1216.

35. Lin JL, Tan DT, Hsu KH, Yu CC. Environmental lead exposure and progressive renal insufficiency. *Arch Intern Med* 2001;161:264-271.

36. Smith NL, Psaty BM, Heckbert SR, Lemaitre RN, Kates DM, Rutan GH, Bleyer A. The association of antihypertensive medication with serum creatinine changes in older adults. *Am J Hypertens* 1997;10:1368-1377.

37. Perrone RD, Madias NE, Levey AS. Serum creatinine as an index of renal function: new insights into old concepts. *Clin Chem* 1992;38(10):1933-1953.

38. Walser M. Assessing renal function from creatinine measurements in adults with chronic renal failure. *American Journal of Kidney Diseases* 1998;32(1):23-31.

39. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976;16:31-41.

40. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. *Annals of Internal Medicine* 1999;130(6):461-470.

41. National Kidney Foundation, K/DOQI Chronic Kidney Disease Evaluation, Classification and Stratification Clinical Practice Guidelines Draft Document. *American Journal of Kidney Diseases* January 2001 (in press).

42. Muntner P, Coresh J, Smith JC, Eckfeldt J, Klag MJ. Plasma lipids and risk of developing renal dysfunction: The Atherosclerosis Risk in Communities Study. *Kidney International* 2000;58:293-301.

43. Zeger SL, Liang KY. Longitudinal analysis for discrete and continuous outcomes. *Biometrics* 1986;42:121-130.

44. Shah BV, Barnwell BG, Bieler GS. 1997. SUDAAN User's Manual, Release 7.5. Research Triangle Park, NC: Research Triangle Institute.