## Supplementary material for:

**Title:** Diabetes, kidney disease and cardiovascular outcomes in the Jackson Heart Study

**Running title:** diabetic kidney disease and cardiovascular disease

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## Supplementary methods:

**Definition of chronic kidney disease:** Urine albumin and creatinine concentrations were measured in clean-catch random (N=2209) or 24-hour (N=1002) urine samples, collected at baseline visit after an overnight fast. There were 276 JHS participants with both 24-hour and spot urine ACR values with a correlation of 0.97. Urine albumin was measured using a human albumin kit (Dade Behring, Neward, Delaware) on a Dade Behring BN II nephelometer. Urine creatinine was measured at the University of Mississippi Medical Center Laboratory Reading Center using a multi-point enzymatic spectrophotometric assay (Vitros CREA dry reaction slides on a Vitros 950 Ortho-Clinical Diagnostics Analyzer, Raritan, New Jersey). Creatinine concentrations were calibrated to the Cleveland Clinic-equivalent Minnesota Beckman CX3 assay.(1) Serum creatinine was measured using the Jaffe method and calibrated to measurements traceable to isotope dilution mass spec (IDMS).(2) Serum cystatin C was measured by a particle-enhanced immunonephelometric assay (N Latex Cystatin C, Siemens AG, Munich). Estimated GFR was calculated from serum concentrations of creatinine and cystatin C measured at baseline using the 2012 CKD-EPI equation.(3)

**Other characteristics:** Demographic and socioeconomic variables (age, gender, income and education) as well as smoking history (never, former, current) were obtained during the baseline interview. Income was derived from family income and size, adjusted by the year of data collection to account for inflation and categorized in four groups (Table 1). Medications used in the two weeks preceding the interview were brought to the clinic and transcribed from bottles and coded by pharmacists using the Medispan dictionary. Blood pressure was measured by trained staff in seated participants after a 5-minute rest, using an appropriately sized cuff and a Hawksley random-zero sphygmomanometer (Hawksley and Sons, Ltd). Two blood pressure readings were taken one minute apart and the arithmetic average was recorded. Hypertension was defined as systolic blood pressure $\geq$140 mmHg, diastolic blood pressure $\geq$90 mmHg and/or

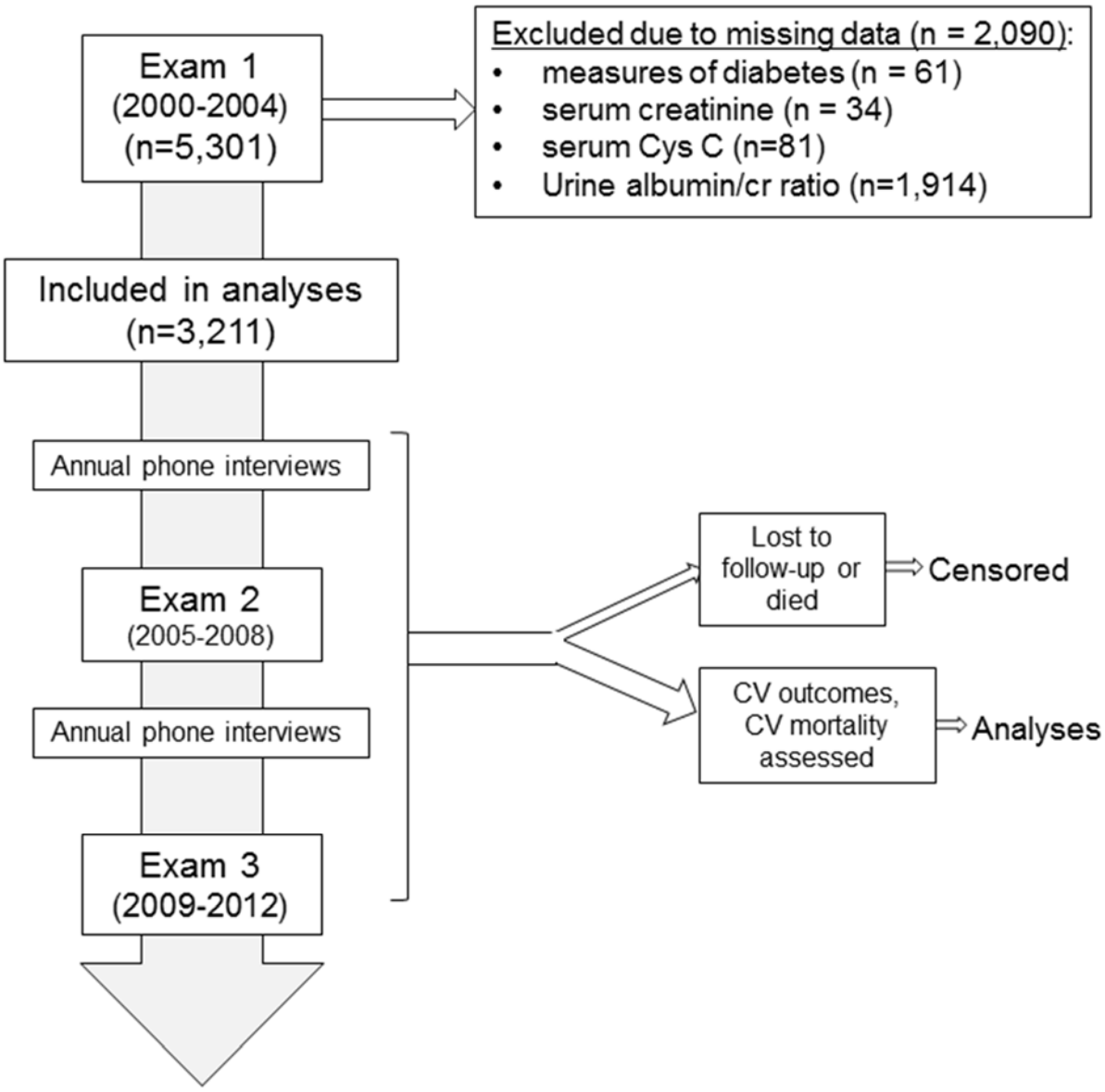
use of antihypertensive medications. Total cholesterol and triglyceride concentrations were measured in fasting blood samples using the Roche enzymatic methods using a Cobras centrifuge analyzer (Hoffman-La Roche).(4) Low-density lipoprotein (LDL) cholesterol concentrations were estimated using the Friedewald formula.(5) Hyperlipidemia was defined as a low-density lipoprotein cholesterol (LDL) $\geq$160 mg/dL and/or use of lipid-lowering medications

**Definition of outcomes:** Incident coronary heart disease was defined as myocardial infarction or need for coronary revascularization, based on data abstracted from medical records, which included presenting symptoms, relevant clinical data (cardiac biomarkers, electrocardiogram, etc) and diagnostic and therapeutic procedures. Adjudicating physicians assigned a diagnosis of no, probable, or definite myocardial infarction based on the abstracted data. For these analyses, probable or definite myocardial infarction was used as part of the coronary heart disease outcome. Incident stroke at outpatient or inpatient settings was defined as cerebrovascular accident due hemorrhagic or ischemic stroke based on review of medical records, including pertinent diagnostic and therapeutic procedures by qualified adjudicating physicians. An incident stroke defined as probable or definite based on this analysis was classified as an event for this outcome. Causes of death were identified by review of ICD-9 codes for the underlying and contributory causes of death, physician (and when indicated coroner or medical examiner) questionnaires, interviews with the next-of-kin and/or any non-family witnesses of death. Deaths from cardiovascular causes were ascertained by review of the causes of death by three physicians (all authors in this manuscript: M.A., N.B. and B.K.) and consisted of the following: acute coronary insufficiency, acute myocardial infarction, acute myocardial ischemia, advanced ischemic cardiomyopathy, (cardiac) arrhythmia, bradyarrhythmia, arteriosclerotic cardiovascular disease, asystole, intracerebral bleeding, cardiac standstill due to severe cardiopathy, cardiogenic failure, cardiomyopathy, cardiovascular events, cerebral hemorrhage, cerebral vascular accident/stroke, complication of cerebral vascular disease, complications of

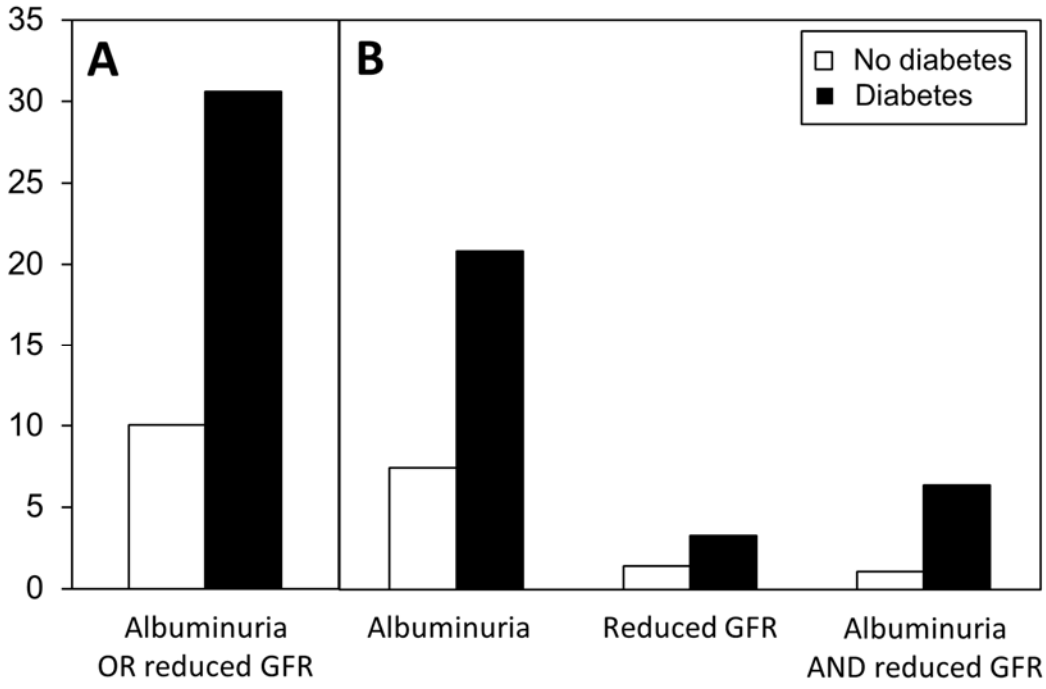
(hypertensive) heart disease, (end-stage) congestive heart failure, consistent with atherosclerotic coronary vascular disease, dissecting abdominal aneurysm, end-stage cardiomyopathy, end-stage heart disease, end-stage stroke, hemorrhagic shock due to abdominal aneurysm, hemorrhagic stroke, history of CVD with chronic decompensation, hypertensive cardiovascular disease, hypertensive heart disease, intracerebral hemorrhage, ischemic cardiomyopathy, ischemic stroke, multiple embolic strokes, myocardial infarction, no cerebral blood flow, possible (or probable) acute myocardial infarction (or insufficiency), probable cardiovascular accident, probable stroke, pulmonary edema and acute left heart failure, severe atherosclerosis with focal occlusive thrombo-embolus, sudden cardiac arrest, ventricular fibrillation, cardiopulmonary arrest, (acute) cardiac arrest.

# SUPPLEMENTARY DATA

**Supplementary Figure 1.** Consort diagram demonstrating the flow of participants whose data was used in these analyses.



**Supplementary Figure 2.** Prevalence (A) and manifestations (B) of kidney disease in people with and without diabetes in the Jackson Heart Study. Closed (■) and open(□) bars indicate people with and without diabetes, respectively.



**Supplementary Table. Baseline characteristics of Jackson Heart Study participants: whole cohort vs. excluded.**

| | Current study | Excluded | Whole Cohort |
|---|---|---|---|
| **Variables** | | | |
| N (%) | 3211 | 2090 | 5301 |
| Age | 54 (13) | 57 (13) | 55 (13) |
| Male | 1218 (38%) | 716 (34%) | 1934 (37%) |
| Income | | | |
| Poor | 354 (13%) | 347 (19%) | 701 (16%) |
| Lower-middle | 611 (23%) | 486 (27%) | 1097 (25%) |
| Upper-middle | 828 (31%) | 497 (28%) | 1325 (30%) |
| Affluent | 882 (33%) | 476 (26%) | 1358 (30%) |
| Smoking | | | |
| Never | 2254 (71%) | 1320 (64%) | 3574 (68%) |
| Former | 555 (17%) | 431 (21%) | 986 (19%) |
| Current | 375 (12%) | 318 (15%) | 693 (13%) |
| SBP (mmHg) | 126 (18) | 128 (19) | 127 (18) |
| DBP (mmHg) | 79 (10) | 78 (11) | 79 (11) |
| Use of anti-hypertensives | 1578 (60%) | 1077 (60%) | 2655 (62%) |
| Hypertension | 1940 (60%) | 1312 (63%) | 3252 (61%) |
| Cholesterol (mg/dL) | 198 (39) | 201 (41) | 199 (40) |
| LDL (mg/dL) | 127 (36) | 127 (37) | 127 (36) |
| Use of HMG-CoA reductase inhibitors | 377 (12%) | 225 (11%) | 602 (11%) |
| Hyperlipidemia | 850 (27%) | 535 (26%) | 1385 (26%) |
| Prevalent cardiovascular disease | 317 (10%) | 255 (12%) | 572 (11%) |
| Creatinine (mg/dL) | 0.92 (0.32) | 0.99 (0.78) | 0.95 (0.54) |
| Cystatin C (mg/L) | 0.74 (0.25) | 0.80 (0.54) | 0.76 (0.39) |
| eGFR (CKD-EPI) | 104 (21) | 99 (23) | 102 (22) |
| ACR (mg/g)* | 6 [4, 13] | 8 [5, 14] | 6 [4, 13] |
| ACR $\geq$ 30 | 399 (12%) | 14/79 (18%) | 413 (16%) |

Data are presented either as numbers (percent), means (SD) or median [interquartile range]. Hypertension and hyperlipidemia were defined as in Table 1. Estimted GFR (eGFR) was calculated as described in Table 1. To convert GFR in ml/min to ml/s, multiply by 0.01667. To convert cholesterol in mg/dl to mmol/L, multiply by 0.0259. SBP: systolic blood pressure; DBP: diastolic blood pressure; LDL: low-density lipoprotein cholesterol; HbA1c: hemoglobin A1c; ACR: Albumin to creatinine ratio.

## References: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