ARIC Manuscript Proposal # 1795

PC Reviewed: 5/10/11  Status: A  Priority: 2
SC Reviewed: _________  Status: _____  Priority: ____

1.a. Full Title: Wrist diameter and diabetes incidence

b. Abbreviated Title (Length 26 characters): Wrist and diabetes

2. Writing Group:
   Writing group members: Aaron Folsom, Rachel Huxley, Pam Lutsey, Liz Selvin, Ellen Demerath, Jim Pankow

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. _AF_____ [please confirm with your initials electronically or in writing]

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ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).
   Name:
   Address:
   Phone:  Fax:
   E-mail:

3. Timeline:
   Will begin soon after approval and try to finish by Fall 2011.

4. Rationale:

   A recent Circulation paper suggested that larger wrist circumference (by MRI) was associated with insulin resistance in overweight/obese children, independent of body fatness (Capizzi M et al. Wrist circumference is a clinical marker of insulin resistance in overweight and obese children and adolescents. Circulation 2011;123:1257-62). Of
course, restricting to fatter children may have contributed to this finding. Nevertheless, the authors offer data and theories on why bone size may reflect insulin and IGF-1 dynamics, which could explain the insulin resistance. Another possible intermediary is osteocalcin (Yeap et al. Eur J Endocrinology 2010 and Tan et al. Metabolism 2011).

ARIC measured wrist diameter at baseline using a sliding caliper, but has not really used the data in manuscripts. Wrist size generally reflects frame size and fat free mass and nearly uncorrelated with body fatness (Himes JH and Bouchard C. Am J Public Health 1985; 75:1076-1079).

5. Main Hypothesis/Study Questions:

Wrist diameter is not associated with incident diabetes, independently of adiposity measures and other risk factors.

The hypothesis is stated as the null, because we actually expect to see no association and contrast this with the Circulation finding mentioned above.

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).

Design: cohort analysis: time to event.

Independent variable: wrist diameter at baseline

Dependent variable: incident diabetes through visit 4, as defined by Pankow in previous analyses. It's based on exam data and uses an interpolated diagnosis date.

Covariates: We therefore will need to carefully control for measures of adiposity (BMI, waist, hip, etc.) and height. Stratification and effect modification testing by sex and race will be explored first, but sex and race may simply be confounders. Other risk factors for diabetes identified in and available for the whole ARIC cohort (e.g., age, SES, physical activity, etc) will be considered for confounding, based on prior ARIC models developed by Pankow and by Raynor. Since wrist is presumably static and measured at baseline, we will probably not need to consider time dependent covariates. Mediation models can be considered, but ARIC did not measure much in the way of potential bone-diabetes mediators. Glucose (HbA1c), insulin, and possibly inflammatory makers are the only ones that come to mind.

Methodologic challenges: Residual confounding by adiposity should not be too concerning, since fatness and wrist are largely uncorrelated. Wrist was assessed by calipers, not MRI, but is pretty accurately measured according to ARIC QC data, so misclassification should be small. Diagnostic suspicion bias or other biases related to differential diabetes detection seem unlikely.
A major issue will be the biological interpretation of any association of wrist circumference with diabetes. ARIC has no data on bone metabolism or structure to help with the interpretation. Wrist size in children, as reported in the Circulation article, may be tracking earlier skeletal growth and maturation, which are associated with increased diabetes risk. In adults, height is associated inversely with diabetes (Weitzman S et al. Acta Diabetol (2010) 47:237–242, and Asao K et al. Diabetes Care 29:1632–1637, 2006) and height may be positively associated with wrist diameter. Those observations would suggest wrist breadth might be inversely, not positively, associated with diabetes, at least univariately.

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

b. If Yes, is the author aware that the file ICTDER03 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?  ____ Yes  ____ No
(This file ICTDER03 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 ICTDER03 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://www.cscu.unc.edu/ARIC/search.php  
__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)?

I did not see any related to wrist measures in ARIC, so there is no overlap.

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?  ____ Yes  __x__ No

11.b. If yes, is the proposal
A. primarily the result of an ancillary study (list number* _________)
B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _________ _________ _________)

*ancillary studies are listed by number at http://www.cscu.unc.edu/aric/forms/

12. 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.