1.a. Full Title: Diabetes and incident Parkinson’s Disease: Results from the ARIC Study

b. Abbreviated Title (Length 26 characters): Diabetes and Parkinson’s Disease

2. Writing Group:
   Writing group members:

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I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. _nmm_ [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).

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3. **Timeline:**

- Sept – Oct 2012: Refinement of analytic plan
- Oct – Dec 2012: Data cleaning and analysis
- Dec 2012 – Jan 2013: Circulate preliminary results to WG
- Jan 2013: Submit abstract for ADA Professional Sessions
- Jan – June 2013: Draft and submit manuscript for publication

4. **Rationale:**

Diabetes is associated with multiple neurologic complications, including neuropathies and dementia. Prior cohort studies conducted in Taiwanese (1) and Finnish populations (2) demonstrate an increased risk of Parkinson’s Disease in patients with type 2 diabetes with adjusted HRs between 1.37 and 1.80. Insulin resistance and hyperinsulinemia may contribute to this increased risk (3). Additionally, plasma uric acid was previously shown to be inversely associated with Parkinson’s Disease in the ARIC Study (4), and diabetes is associated with lower uric acid levels (unpublished; MS1933). The relationship between dysglycemia and Parkinson’s Disease in the United States, including in African Americans, remains unknown.

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

1. Prevalent type 2 diabetes is associated with incident Parkinson’s Disease.

2. Hemoglobin A1c is positively associated with incident Parkinson’s Disease.

3. Fasting glucose and fasting insulin are positively associated with incident Parkinson’s Disease.

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:** prospective cohort  
**Inclusion criteria:** Data on diabetes or fasting glucose status  
**Exclusion criteria:** Prevalent Parkinson’s Disease  
**Independent variables:** Diabetes (visit 1), hemoglobin A1c (visit 2), fasting glucose (visit 1), fasting insulin (visit 1)  
**Main outcome:** Incident Parkinson’s Disease based on ICD-9 codes at hospital discharge as previously defined and validated in ARIC (2009.19)  
**Data analysis:** Cox proportional hazards modeling to determine the independent effect of type 2 diabetes, HbA1c, fasting glucose, and fasting insulin on incident Parkinson’s Disease; sex-stratified analyses  
**Covariates:** Site, age, sex, race/ethnicity, education, income, employment, body weight, blood pressure, lipids, uric acid, alcohol intake, physical activity, caffeine intake, smoking, and insulin use
Limitations/challenges anticipated: Power limited by prevalent cases of diabetes and incidence of Parkinson’s Disease

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 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? _x__ 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.csc.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)?

MS1176: Lower LDL-Cholesterol is associated with Parkinson’s disease: results from ARIC Study participants (Chen, H)

MS1299: Uric acid and Parkinson’s Disease in ARIC (Am J Epidemiol, 2009 May 1;169(9):1064-9. Epub 2009 Mar 18; (4))

MS1933: The association between serum uric acid, diabetes risk, and diabetes duration (Jurashcek, S)

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? _x__ Yes ___ No
11.b. If yes, is the proposal
   _x_   A. primarily the result of an ancillary study (list number* __2009.16, 2009.19_)
   ___   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.cscc.unc.edu/aric/forms/

12a. 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.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is your responsibility to upload manuscripts to PUBMED Central whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to Pubmed central.