ARIC Manuscript Proposal #2914

PC Reviewed: 12/13/16 **Status: _____** **Priority: 2**
SC Reviewed: _____ **Status: _____** **Priority: ____**

1.a. Full Title: Periodontal Profile Class (PPC), Index of Periodontal Classes (IPC) Associated with incident diabetes

b. Abbreviated Title (Length 26 characters): **Perio PPC Incident Diabetes**

2. Writing Group:
Writing group members:
Steven Offenbacher, Jim Pankow, Thiago Morelli, John Preisser, Kevin Moss, Jim Beck, Others?

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __SO___ **[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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We invite ARIC investigator(s) to participate in this manuscript

3. Timeline: Six-nine months for manuscript draft.

4. Rationale: The association between diabetes and periodontal disease has been studied extensively for over 50 years predominantly in cross-sectional studies, with few longitudinal analyses. Most studies recognize this as a bidirectional relationship. Our intention is to report the associations with the newly developed Periodontal Profile Classes (PPC) and Index of Periodontal Classes (IPC) and Incident Diabetes. To date there have been no reports of the relationship between PPC/IPC and incident T2DM . Genco and colleagues have shown in longitudinal cohort studies that individuals with both diabetes and severe periodontal disease are at much higher risk for diabetes-associated complications and increased mortality due to cardiovascular events.

A robust periodontal disease classification has been elusive for many years. We have developed seven Periodontal Profile Classes (PPC), seven Tooth Profile Classes (TPC). These classes were developed agnostically using Latent Class Analysis (LCA) to improve our ability to predict tooth loss and incident periodontal disease, as compared to previous disease classifications (e.g. CDC/AAP). By definition LCA creates unique non-overlapping groups/classes of people (or teeth). These classes represent groups of people (or teeth) that can be described by generally accepted patterns of periodontal disease classifications found in the general population. We have demonstrated these are robust definitions of oral conditions when harmonized to other datasets and have recently published the LCA method for periodontal disease classification. In addition we have developed an Index of Periodontal Classes (IPC). IPC is calculated by mean TPC scores weighted by risk of tooth loss within each level of PPC (manuscript in preparation under an approved ARIC manuscript proposal #2874). We believe the use of tooth loss weights in calculating IPC captures the risk of future tooth loss, as well as attachment loss, and may be related to prevalent or incident systemic disease events. Importantly, this is the first periodontal disease classification system that includes missing teeth patterns. Furthermore, we have found these measures to be useful definitions of disease for developing risk models for dental outcomes and other conditions.

5. Main Hypothesis/Study Questions: Periodontal Profile Classes (PPC) and Index of Periodontal Classes (IPC) are associated with incident T2DM.

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).

Our analysis will use PPC and IPC as exposures and incident diabetes as the outcome. We will exclude individuals with prevalent diabetes at visit 4 (self-reported physician diagnosis, self-reported diabetes medication use, fasting glucose of 126 mg/dL or higher, non-fasting glucose of 200 mg/dL or higher, or 2-hour glucose of 200 mg/dL or higher following the oral glucose tolerance test) We will define incident diabetes based on physician diagnosis and diabetes medication use reported during annual telephone interviews between visits 4 and 5, along with fasting glucose and hemoglobin A_{1c} values measured at visit 5. We will utilize Cox proportional hazards models, with time of event defined as the date of diabetes ascertainment. We plan to use age, race/center, sex, blood pressure, hypertension medications, lipids, smoking, BMI, waist circumference, and education as control variables where appropriate. The dental variables were

collected at ARIC Visit 4 from the Dental Ancillary Study. We will use ARIC Visit 4 data where ever possible. .

The dental team currently has all the visit 4 dental variables needed for the analysis but does not have the ARIC Visit 5 data. We will request ARIC Visit 5 once the manuscript proposal is approved. The dental team will be responsible for the analysis.

We have no preliminary data showing a relationship between PPC/IPC and incident diabetes. Periodontal disease is strongly associated with prevalent diabetes and pre-diabetes as well as insulin resistance and HOMA scores in the ARIC dataset [data not shown]. Our hypothesis is that PPC and/or IPC is independently associated with incident diabetes
We may contrast our exposures showing AAP/CDC definition of periodontal disease, PPC and IPC and their relationships to incident diabetes. We believe PPC/IPC will be a better predictor of incident diabetes than the AAP/CDC standard definition of periodontal disease. This is because it is a better whole mouth assessment of infectious risk because it includes periodontal disease and caries and is predictive of periodontal disease progression and tooth loss that are important markers of systemic challenge.

7.a. Will the data be used for non-CVD analysis in this manuscript? __ __ Yes __X*__ No
***we realize diabetes is a major risk factor for CVD and some may consider it a CVD analysis.**

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 ICTDER 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.cscc.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)?
There are many manuscript proposals that use dental variables as an exposure including but not limited to #492, 687, 861, 730, 827, 858, 913, 915, 929, 995, 1112, 1284, 1892, 2053 and 1859.

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* __ 1996.01_)
___ 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.

13. Per Data Use Agreement Addendum, approved manuscripts using CMS data shall be submitted by the Coordinating Center to CMS for informational purposes prior to publication. Approved manuscripts should be sent to Pingping Wu at CC, at pingping_wu@unc.edu. I will be using CMS data in my manuscript ____ Yes __X__ No.