ARIC Manuscript Proposal #2890

PC Reviewed: 11/08/16 **Status: _____** **Priority: 2**
SC Reviewed: _____ **Status: _____** **Priority: ____**

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

b. Abbreviated Title (Length 26 characters):
Perio PPC Prevalent CVD

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

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

First author:
Address: James D Beck
UNC School of Dentistry
Chapel Hill, NC 27302

Phone: 919-537-3241 Fax:
E-mail: Jim_Beck@unc.edu

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: Gerardo Heiss (if he will accept)
Address:

Phone: Fax:
E-mail:

We invite ARIC investigator(s) to participate in this manuscript

3. Timeline: About six-nine months for manuscript draft. Preliminary analysis has already been started. We plan to submit the manuscript on incident CVD events prior to this manuscript.

4. Rationale: For many years the Dental Team from the ARIC dental ancillary study have proposed that periodontal disease is associated with CVD. There have been many conflicting reports in the literature on this association. One of the major issues in the dental research field is that there is currently no generally accepted definition of periodontal disease used for research. This is not unique to the periodontal field different definitions of the exposure can be found in many fields of medicine, especially in complex diseases. Periodontal disease was first described by Fauchard in 1723 when he used the term "scurvy of the gums". Since then researchers have introduced many different names for periodontal disease. These definitions of periodontal disease use different clinical criteria many of which have been subjective. An example can be found in the attached document (UNC-School of Dentistry Diagnosis, Classification and Treatment Chart for Most Common Periodontal Diseases). This document currently being used in the UNC-School of Dentistry uses seven different overlapping clinical criteria (bleeding on probing, suppuration, CAL, PD, mobility, furcation and radiographic alveolar bone loss) and uses terms like "and/or", "slightly higher", "slightly less", "usually but not necessarily", "about", "sometimes". Periodontal literature uses both these subjective and objective definitions of disease. Often when objective definitions of periodontal disease are used in literature the definitions are different than what other reports use. We feel this leads to one of the sources of variation that can cause conflicting reports.

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). Although we have already published one paper on periodontal disease and prevalent CHD with non-significant findings with clinical signs of periodontal disease [Circulation 2005, Beck etal.], 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 related to Prevalent CVD.

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 Prevalent CVD as the outcome. We plan to use age, race/center, sex, diabetes, hypertension, lipids, smoking, BMI, and education as control variables. These variables were collected at ARIC Visit 4 from the Dental Ancillary Study. We plan to replicate of our findings, where possible, using the National Health and Nutrition Examination Survey (NHANES). NHANES included full mouth oral examinations in the 2009-2010, 2011-2012 and 2013-2014 examination cycles. Our plan is to combine the three NHANES exam cycles (n=~10,000). We feel utilizing both the Dental ARIC and NHANES studies to report the relationship of PPC/IPC and Prevalent CVD will enhance the manuscript. Preliminary data from the NHANES study are shown in Table 1 below.

The dental team currently has all the dental variables needed for the analysis and will be responsible for the analysis.

Table 1: Proposed Table:
Adjusted Odds Ratio (CI) for Prevalent Cardiovascular Outcomes by IPC Continuous (every 10 units of change), Quartiles of IPC and PPC.

IPC	Dental ARIC	NHANES (n=10,042)	Prevalence Model Improvement* Dental ARIC/NHANES
	Ever Told You have CHF	Ever Told You have CHF	
Continuous		1.20 (1.03-1.39)	../5.4
Quartile 1		Ref	../8.4
Quartile 2		1.47 (0.89-2.42)	
Quartile 3		1.72 (1.16-2.54)	
Quartile 4		1.60 (1.08-2.38)	
PPC-A		Ref	../13.1
PPC-B		0.54 (0.21-1.37)	
PPC-C		1.28 (0.80-2.04)	
PPC-D		1.43 (0.95-2.15)	
PPC-E		1.53 (0.76-3.05)	
PPC-F		1.90 (1.23-2.93)	
PPC-G		1.29 (0.72-2.33)	
	Prevalent MI	Ever Told You Had Heart Attack	
Continuous		1.16 (1.02-1.31)	../5.0
Quartile 1		Ref	../9.0
Quartile 2		1.26 (0.82-1.93)	
Quartile 3		1.58 (1.13-2.20)	
Quartile 4		1.56 (1.11-2.18)	
PPC-A		Ref	../18.2
PPC-B		0.79 (0.40-1.55)	
PPC-C		1.34 (0.90-1.99)	
PPC-D		1.52 (1.07-2.16)	
PPC-E		2.45 (1.51-3.96)	
PPC-F		1.64 (1.11-2.42)	
PPC-G		1.41 (0.88-2.27)	
	Prevalent Stroke	Ever Told You Had A Stroke	
Continuous		1.28 (1.12-1.47)	../13.0

Quartile 1 Quartile 2 Quartile 3 Quartile 4		Ref 1.37 (0.85-2.20) 2.09 (1.47-2.97) 1.91 (1.33-2.74)	../19.6
PPC-A PPC-B PPC-C PPC-D PPC-E PPC-F PPC-G		Ref 0.89 (0.42-1.86) 1.53 (1.00-2.34) 1.94 (1.34-2.80) 2.06 (1.15-3.69) 2.22 (1.49-3.31) 1.54 (0.91-2.60)	../22.7

Adjusted for Race, Age, Gender, Smoking, Diabetes, Hypertension, BMI, Total Cholesterol and HDL
*Model Improvement in Prevalent disease with and without the PPC/IPC showing Change in Bayes Factors (BIC) (0-2 weak, 2-6 Positive, 6-10 Strong, 10+ Very Strong – Raftery criteria)

We may contrast our exposures showing AAP/CDC definition of periodontal disease, PPC and IPC and their relationships to prevalent CVD.

CVD will include CHF, Stroke, MI, and others.

This manuscript proposal will focus on PPC/IPC → prevalent CVD relationships. Other proposals are being submitted for PPC/IPC → incident events, PPC/IPC → risk factors of CVD (including Diabetes, Serum C-Reactive Protein, HDL, Obesity, Thick IMT and Calcification).

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 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 ____ No.

University of North Carolina at Chapel Hill School of Dentistry
Diagnosis, Classification, and Treatment Chart for the Most Common Periodontal Diseases

A Guideline for *Predoctoral Dental Students* Healthy Periodontium (Type N)	**Dental Plaque-Induced Gingivitis† (Type I)**	***Slight* Chronic Periodontitis†† (Type II)**	***Moderate* Chronic Periodontitis†† (Type III)**	***Severe* Chronic Periodontitis†† (Type IV)**
No bleeding upon probing	Presence of bleeding and/or suppuration upon probing	Presence of bleeding and/or suppuration upon probing	Presence of bleeding and/or suppuration upon probing	Presence of bleeding and/or suppuration upon probing
CAL = 0 mm	CAL = 0 mm	CAL = 1 or 2 mm	CAL = 3 or 4 mm	*CAL ≥ 5 mm*
PD = mostly 1-3 mm	PD = mostly 1-3 mm or slightly higher	PD = mostly 3-4 mm or slightly higher	PD = mostly 5-6 mm or slightly higher	PD ≥ 7mm mostly or slightly less
No mobility	No mobility usually	No mobility usually	Mobility I usually but not necessarily	Mobility II and III usually but not necessarily
No furcation	No furcation	No furcation usually	Furcation I usually or II sometimes	Furcation II or III mostly but not necessarily
No radiographic alveolar bone loss	No radiographic alveolar bone loss	Radiographic alveolar bone loss ~ 1-2 mm	Radiographic alveolar bone loss ~ 1/3 of root	Radiographic alveolar bone loss > 50% of root Vertical (angular) alveolar bone loss