1. a. Full Title: Relationship between Periodontitis and Hypertension.

b. Abbreviated Title (Length 26 characters): Periodontitis and High BP

2. Writing Group:
   Writing group members: Valentine Oluchi, F. Javier Nieto, James D. Beck, Steve Offenbacker.

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

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3. Timeline: Obtain data set September 2007:  
Begin statistical analysis September 2007:  
Complete statistical analysis December 2007:  
Submit IADR abstract April 2008:  
Complete manuscript May 2008:  
4. **Rationale:**

Inflammation has been linked to the development of diseases of the cardiovascular system. The development of atherosclerosis involves a chronic low grade inflammation occurring within the arterial wall. (1, 2) Several studies have shown an association between blood levels of inflammatory markers and the development of cardiovascular disease. (3) Infections are associated with atherosclerosis (4) and some studies have shown that infections are associated with coronary heart disease (5) and also with carotid intimal-medial thickening. (6) Mild chronic inflammation may play a significant role in the incidence of high blood pressure. By impairing the capacity of the endothelium to generate vasodilating factors, particularly nitric oxide (NO), elevated cytokines may lead to the development of endothelial dysfunction, chronic impaired vasodilation, and high blood pressure. (7, 8) Several studies have shown an association between blood levels of markers of inflammation and hypertension. (9,10,11,12)

Studies have also shown an association between periodontitis and systemic markers of the acute phase response. (13,14,15) These findings suggest that the increased levels of systemic acute phase reactants such as C-reactive protein resulting from the inflammatory process associated with periodontitis may be a link between periodontitis and hypertension.

A randomized controlled trial using 120 patients found that the benefits in oral health from treatment of periodontitis were associated with improvement in endothelial function. (16) Another study using 424 subjects found an association between periodontitis and hypertension (17) and a larger study based on 4,254 subjects also found that the severity of periodontal disease was related to hypertension independent of age. (18)

5. Main Hypothesis/Study Questions:
The purpose of this study is to determine if there is an association between clinical measures of periodontitis and Hypertension at visit 4 in the ARIC study while controlling for potential confounding variables. Also longitudinal data will be analyzed using the ARIC MRI sample of 2000 participants. Appropriate sampling weights will be applied because of the over-sampling according to carotid IMT in the ARIC MRI sample.

Hypothesis 1: More severe levels of periodontitis are associated with higher levels of blood pressure.

Hypothesis 2: Incidence of hypertension is higher in subjects with periodontitis compared with subjects without periodontitis.

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).

Data (variables, time window, source, inclusions/exclusions):
Include all persons with a clinical periodontal examination, and measurement of blood pressure at ARIC visit 4. Add follow-up blood pressure and covariate data from the ARIC MRI sample.

Main Exposures: Periodontal disease attachment loss extent, pocket depth extent, bleeding on probing. [The definition of the main exposure will be based on pocket depth and bleeding on probing because we are interested in an exposure definition that better represents both the clinical and biological features of periodontitis.]

Dependent variables: Cross-sectionally and prospectively assessed (ARIC MRI sample) Systolic blood pressure, Diastolic blood pressure, hypertension status (SPB/DBP >=140/90 or antihypertensive medications).

Covariates: Sex, race, field center, age, household income, educational status, diabetes, physical activity, BMI, smoking status, leukocyte count, fibrinogen, lipid levels, serum C-Reactive Protein, brushing/flossing behaviors, dental visit behavior, method of financing dental care.
Potential effect modifiers: Level of physical activity, Smoking status and intensity, obesity (derived from BMI).

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 ICTDER02 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 ICTDER02 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

    b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER02 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)?


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

    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.cscc.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.