

ARIC Manuscript Proposal # 995

PC Reviewed: 02/25/04
SC Reviewed: 02/25/04

Status: A
Status: A

Priority: 2
Priority: 2

1.a. Full Title: Periodontal Disease and Coronary Heart Disease: A Tale of Two Exposure Measures.

b. Abbreviated Title (Length 26 characters):
Periodontitis, antibodies and CHD

2. Writing Group (list individual with lead responsibility first):

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3. Timeline:

MS Proposal #687 was very general, including many aspects of periodontal disease with CHD and IMT. The manuscript published under that number involved clinical periodontal disease and IMT. This proposed manuscript concentrates on the relationship of both clinical signs of periodontal disease and antibodies to oral organisms with prevalent CHD. Rather than splitting MS proposal #687 into multiple manuscripts we would like to request a different manuscript number for this paper. The data analyses for this manuscript are almost complete. Thus, the manuscript can be submitted to the ARIC Publications Committee sometime during April, 2004.

4. Rationale:

Some studies have reported significant positive associations between periodontal disease and CHD, while others have not. Speculations regarding reasons for this variability have included the suggestion [1] that since the clinical signs of periodontal disease are a consequence of the interaction between the infectious microorganisms and the host immune and inflammatory response, it is likely that including measurement of this interaction would be a more direct measure of the systemic component of the periodontal exposure that is a consequence of periodontal disease. Evidence in support of this concept has been recently provided by Pussinen [2] who demonstrated that the presence of serum IgG-antibodies to *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis* was associated with CHD adjusting for age and several CHD risk factors. A second major criticism of the data linking CVD to periodontitis focuses on the role of smoking. Smoking is accepted as a risk factor for both periodontal disease and heart disease and must be considered as a confounder of any periodontal disease – heart disease association. While most studies have controlled for smoking by means of multivariable analyses, Hujoel and his colleagues have focused on the possibility that smoking has such a strong influence on both diseases that statistical control cannot completely adjust for

its effects and stratification on smoking is needed [3-6]. In fact, these investigators hypothesize that both periodontal disease and heart disease are co-morbid conditions that result from smoking. Certainly, these points on confounding and stratification raise important considerations worthy of further study. The aim of this study is to describe the relationship between a case-based definition of periodontal disease (Healthy, early periodontitis, severe periodontitis) and CHD as well as the relationship between serum IgG antibodies to 17 oral organisms and prevalent detected CHD.

1. Beck, J. and S. Offenbacher, *Relationships among clinical measures of periodontal disease and their associations with systemic markers*. *Ann Periodontol*, 2002. 7: p. 79-89.
2. Pussinen, P., et al., *Antibodies to periodontal pathogens are associated with coronary heart disease*. *Arterioscler Throm Vasc Biol*, 2003. 23(7): p. 1250-1254.
3. Hujoel, P., et al., *A hidden periodontitis epidemic during the 20th century?* *Community Dent Oral Epidemiol*, 2003. 31(1): p. 1-6.
4. Hujoel, P., et al., *An exploration of the periodontitis - cancer association*. *Ann Epidemiol*, 2003. 13(5): p. 312-316.
5. Hujoel, P., et al., *Periodontitis - systemic disease associations in the presence of smoking --causal or coincidental?* *Periodontol 2000*, 2002. 30: p. 51-60.
6. Hujoel, P., *Does chronic periodontitis cause coronary heart disease? A review of the literature*. *J Am Dent Assoc*, 2002. 133 Suppl: p. 31S-36S.

5. Main Hypothesis/Study Questions:

Four hypotheses to be tested are:

Periodontal case status (Healthy, early periodontitis, severe periodontitis) is associated with prevalent CHD, adjusting for relevant confounders.

The association between antibody levels and CHD will be restricted to current and former smokers **when stratifying on ever (current and former) and never smokers**.

High serum antibody IgG levels (above the Median) to oral organisms will be positively associated with the prevalent CHD, adjusting for relevant confounders.

The association between antibody levels and CHD will be restricted to current and former smokers **when stratifying on ever (current and former) and never smokers**.

6. Data (variables, time window, source, inclusions/exclusions):

The data needed for this manuscript are already available. We plan to use only detected cases for our outcome measure (prevalent CHD at visit 4). Thus, will ignore reported CHD at baseline and only use diagnoses of CHD detected at an ARIC exam or through community surveillance between visits 1 and 4. Participants included in the study would have had periodontal examinations at visit 4, have serum samples available for assaying IgG antibodies, and information on potential confounders.

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

8.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://bios.unc.edu/units/csc/ARIC/stdy/studymem.html>

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)? See explanation under Timeline. MS #915, Clinical Periodontal Disease and Self-reported vs Detected CHD, also pertains to this study. That MS is currently being reviewed by the writing group.