

# Periodontal Disease, Cardiovascular Disease, the American Heart Association, the American Academy of Periodontology, and the Rooster Syndrome

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## Background

An April 2012 systematic review examining the relationship of periodontal disease and cardiovascular disease, and published in the American Heart Association's (AHA) journal *Circulation*<sup>1</sup>, created a significant stir in the popular press and the oral health community.

The controversy appears to arise from differences in emphasis in two key sentences that frame the take home message in the systematic review. These sentences occur sequentially and adjacent to one another in the abstract.

1. "Observational studies to date support an association between PD [periodontal disease] and ASVD [atherosclerotic vascular disease] independent of known confounders."
2. "They do not, however, support a causative relationship."

The American Academy of Periodontology's (AAP) press release focused on the first sentence with this headline: "Periodontal Disease Linked to Cardiovascular Disease".

The press release goes on to state: "... observational studies to date support an association between periodontal disease and cardiovascular disease, independent of shared risk factors. The AHA's statement confirms the conclusions of the statements published by the AAP and the *American Journal of Cardiology* in 2009 and the U.S. Preventive Services Task Force in 2008." (<http://www.perio.org/consumer/AHA-statement.htm>)

This press release was picked up by some news outlets who focused on sentence 1, with headlines taken directly from the American Academy of Periodontology: "Periodontal Disease Linked to Cardiovascular Disease" (eg: US Newswire, April 18, 2012 [www.prnewswire.com/news-releases/periodontal-disease-linked-to-cardiovascular-disease-147980725.html](http://www.prnewswire.com/news-releases/periodontal-disease-linked-to-cardiovascular-disease-147980725.html)).

Other news sources, quoting a press release from report's senior author focused on sentence 2, with the following headline: "No Proof that Gum Disease Causes Heart Disease" (eg: MedlinePlus: [http://www.nlm.nih.gov/medlineplus/news/fullstory\\_124229.html](http://www.nlm.nih.gov/medlineplus/news/fullstory_124229.html)).

The American Heart Association attempted to clarify this apparent controversy on their website with the following bullet points ([http://my.americanheart.org/professional/General/Periodontal-Disease-and-Atherosclerotic-Vascular-Disease\\_UCM\\_439029\\_Article.jsp](http://my.americanheart.org/professional/General/Periodontal-Disease-and-Atherosclerotic-Vascular-Disease_UCM_439029_Article.jsp)):

- There is an association between periodontal disease and atherosclerotic vascular disease.
- It has not been demonstrated that periodontal disease is a cause of atherosclerotic vascular disease.
- It is not confirmed that heart disease or stroke can be prevented, or the clinical course of atherosclerotic vascular disease modified, by therapeutic periodontal interventions.

And still other headlines extrapolated from sentence 2: "Gum disease heart link 'a myth' (eg: Herald United Kingdom, April 19, 2012 [www.heraldsotland.com/news/home-news/gum-disease-heart-link-a-myth.17344541](http://www.heraldsotland.com/news/home-news/gum-disease-heart-link-a-myth.17344541)).

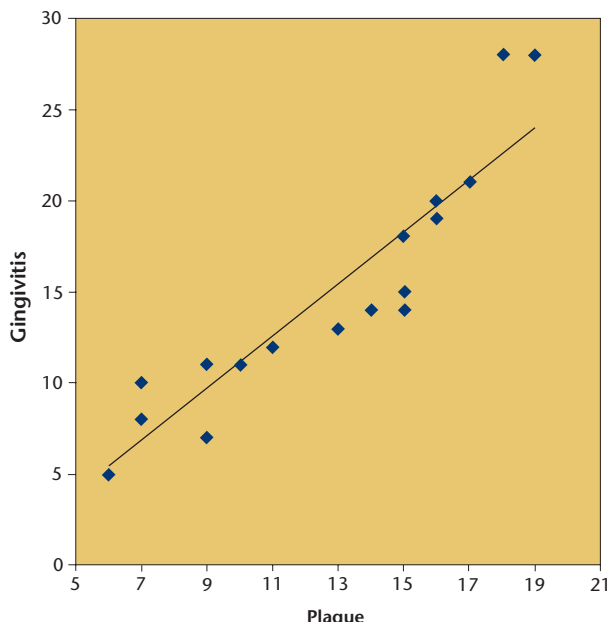
The controversy brings to mind the story that the rooster's crowing causes the sun to rise. Or more formally, post hoc ergo propter hoc (after this, because of this) and its corollary cum hoc ergo propter hoc (with this, because of this).

For comparison, and more simply, one might consider the well regarded relationship of plaque and gingivitis (Figure 1). Were these the only data set one had, one might normally provide a patient with a prophylaxis and oral hygiene instruction to reduce gingivitis. The concept is that if one reduces the contributor to disease (plaque), one can reduce the disease (gingivitis). However, an alternate look at the same data set might change ones view of the presumed cause-effect relationship (Figure 2).

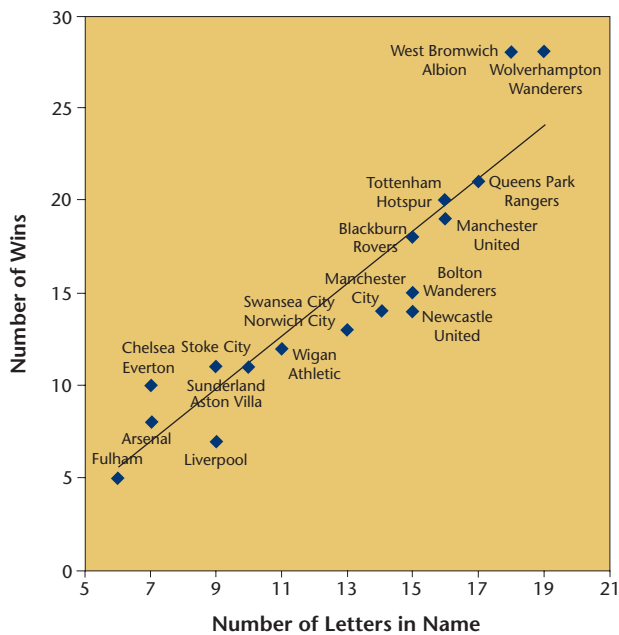
## Why the controversy?

As oral health students, most of us learned Koch's four postulates for demonstrating disease causation from unitary bacterial infections. Bradford-Hill<sup>2</sup> postulates provided a new approach to assess causation for more complex diseases. His seven postulates can be used to examine the relationship between periodontal disease and cardiovascular disease.<sup>1,3</sup>

1. **Temporal Relation.** The temporality argument is not well established for periodontal disease preceding cardiovascular disease. Most studies looking at this are cross sectional, demonstrate a significant correlation (see Figures 1 and 2), but cannot establish a pre/post temporal relationship. This weakens the argument for a cause-effect relationship, and has led to most of the confusion.
2. **Strength of Association.** The odds ratios for periodontal disease-cardiovascular disease association are in the range of 1.5 to more than 5. These may seem large, but not large enough to differentiate association from cause-effect.
3. **Dose Response.** The question is: Is worse periodontal disease associated with a greater prevalence or severity of cardiovascular disease? A few association studies support a dose response, but most do not adequately address this question.
4. **Consistency.** This is an interesting question, and would require an assessment of publication bias. That is, how many studies that did not find an association were not published either by the authors decision or the reviewer's/editor's decision?
5. **Plausibility and Coherence.** Clearly there is biological plausibility. Multiple biological, animal, and human examples of disease demonstrate that for both periodontal disease and cardiovascular disease, there is a relationship between



**Figure 1. Relationship of plaque and gingivitis. The solid line is the linear regression, and the correlation coefficient is 0.7.**



**Figure 2. Relationship of Letters in to Premier League Name to Wins. The solid line is the linear regression, and the correlation coefficient is 0.7. This chart is identical to Figure 1, but with actual team names and predicted 2013 wins. The probability that the number of letters in the team name would predict the wins is questionable. (adapted from: Norman and Streiner, 19984)**

inflammation and/or bacterial infection and disease prevalence and severity. However there are several studies that show completely edentulous people (and therefore have no current, but may have had previous periodontal disease) have as much risk for cardiovascular disease as do people with periodontal disease. This argues for a common risk factor model for both periodontal disease and cardiovascular disease, but not a causal relationship.

**6. Specificity.** Is this a single putative cause? Clearly not. It would be interesting to see how other "inflammatory" conditions (rheumatoid arthritis, lupus, etc.) fit into the model of common risk factors. In other words, are these other inflammatory

conditions also associated with periodontal disease and cardiovascular disease? If they were, this would weaken the concept that periodontal disease causes cardiovascular disease. Conversely, finding that multiple inflammatory or infectious diseases increase the risk of cardiovascular disease would strengthen the argument that periodontal disease increases the risk of cardiovascular disease.

**7. Consideration of Alternative Explanations.** This is where the oral health community currently finds itself. There are some that think the periodontal-cardiovascular disease relationship is a residual confounding effect from other common health risk factors (e.g., smoking). Others think that there is an underlying common risk factor (e.g.: genetic based predisposition for both conditions). Both are reasonable explanations, and both would require experimental trials to demonstrate cause-effect. However, we can't randomly assign people to smoke or not and we have yet to find the gene(s). So, at best, we can do a treatment experiment, where we see if those who have their periodontal disease effectively treated (reducing both the infection and the inflammation) demonstrate a reduced risk of cardiovascular disease. No trials have yet been registered or reported that coordinately address all for issues (periodontal disease, cardiovascular disease, infection, and inflammation). The intervention trials that have been done to address the periodontal disease, to date, have focused on mechanical therapy and clinical outcomes. They have not, however, quantitatively examined infection and inflammation.

**Summary**

Returning to the two key sentences from the Abstract of Lockhart *et al*,<sup>1</sup> the studies linking periodontal disease to cardiovascular disease, to date, are largely association studies. Therefore, sentence 1 is accurate: These studies "... support an association between PD and ASVD independent of known confounders."

The issue with association studies is that the association may either accurately or spuriously portray a cause-effect relationship (see Figures 1 and 2). Said differently, association studies generate hypotheses that need to be tested.

Sentence 2, however, might be more accurate were it so include two more words: "They do not, however, support [or refute] a causative relationship." In other words, the final word isn't in. A determination of a cause-effect relationship will require an intervention trial, as indicated in the seventh of Hill's postulates.

Taken together, this suggests that the rooster(s), perhaps, might consider whether it wants to crow before or after sun up, and the clinical trials are completed, to avoid confusion.

1. Lockhart PB, Bolger AF, Papapanou PN, *et al*; on behalf of the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, Council on Epidemiology and Prevention, Council on Peripheral Vascular Disease, and Council on. Periodontal Disease and Atherosclerotic Vascular Disease: Does the Evidence Support an Independent Association?: A Scientific Statement From the American Heart Association. *Circulation*. 2012. 22; **125**: 2520–2544.
2. Bradford-Hill A. "The Environment and Disease: Association or Causation?". *Proceedings of the Royal Society of Medicine* 1965; **58**: 295–300.
3. Friedewald VE, Kormman KS, Beck JD, Genco R, Goldfine A, Libby P, Offenbacher S, Ridker PM, Van Dyke TE, Roberts WC. The American Journal of Cardiology and Journal of Periodontology Editors' Consensus: Periodontitis and Atherosclerotic Cardiovascular Disease. *Am J Cardiol* 2009; **104**: 59–68.
4. Norman GR, Streiner DL. *PDQ Epidemiology*. 1998. BC Decker, London.

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