

## The importance of assessing confounding and effect modification in research involving periodontal disease and systemic diseases

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## **Guest Editorial**

Focused Perspective on Yiöstalo et al., J Clin Periodontol 2006; 33: 105–109

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This issue includes an interesting and timely paper by Ylöstalo and Knuuttila that explores the concepts of confounding and effect modification. It illustrates the importance of recognizing and properly accounting for them in the design and analysis of studies of periodontal diseases.

Confounding and effect modification are of increasing importance as periodontal research addresses the putative associations between periodontal disease and systemic diseases. This is especially pertinent when dealing with smoking as smoking is a major risk factor for both periodontal disease and a number of systemic diseases. As a result, it is very difficult to disentangle the effects of smoking and periodontal disease in studies of systemic diseases (Spiekerman et al. 2003). Moreover, smoking has already been identified as an effect modifier in the associations between periodontal disease and both coronary heart disease and chronic obstructive pulmonary disease (Hyman et al. 2002, Hyman & Reid 2004).

Unfortunately, the importance of confounding and effect modification are not always appreciated and are often overlooked. They may also appear to be similar but they are actually very different. Our goals in controlling them are also different. "In epidemiologic analysis one tries to eliminate confounding, but one tries to detect and estimate effect-measure modification.'' (Rothman & Greenland 1998, p. 254). We also assess effect modification first, since confounding by a variable becomes largely irrelevant if there is also interaction involving that variable (Kleinbaum 1994, p. 166).

Confounding results from imbalances in risk factors for the study outcome in different exposure groups (Rothman 2002, p. 110). It can be dealt with in the design of prospective studies by randomization or, in the case of known confounders, by restriction of the study population based on the confounding variable. For example, a study could be limited to females. In a regression analysis, confounding variables can usually be adequately handled by including them in the model, if there is overlap in the confounding variables among the exposed and unexposed population. So in a study of periodontal disease and heart disease, we could adjust for confounding by gender if there were both males and females among those with and without periodontal disease.(Rothman 2002, p. 190) However, if a confounding variable is biased (i.e. the data is inaccurate) it may not be possible to completely adjust for the effects of confounding. In this situation, it can become very difficult to differentiate between confounding and Accepted for publication 11 November 2006

effect modification (Spiekerman et al. 2003).

Effect modification occurs when the effect of the risk factor on an outcome differs depending on the value of another variable (Katz 2003). It has been given multiple names, interaction, effect modification, and effect measure modification. It also requires a formal statistical test to detect it. It can only be adequately dealt with at the analysis stage by including interaction terms in the model or stratifying the analysis based on the interaction variable. It is also model (or scale) dependent and may vary across the range of values of the effect modifier (Starr & McNight 2004).

Given these many analytic difficulties, the temptation to ignore effect modification can be great. However as Kleinbaum et al. (1982, p. 448) state "the failure to detect and quantify the key interaction effect in the data can lead to serious errors in interpreting the exposure-disease relationships under study."

As an example, a recent study found an association between advanced periodontal disease and self reported coronary heart disease. However, after stratifying by smoking status the association was limited to smokers (Hyman et al. 2002). In this study, ignoring effect modification would have resulted in a faulty analysis and incorrect inferences. Very few papers addressing periodontal disease and systemic diseases mention an assessment of effect modification. It is possible that this type of analytic error is common in the literature.

As Ylöstalo and Knuuttila discuss, we will not be able to properly understand the relationships between periodontal disease and systemic diseases unless future researchers fully assess potential confounding and effect modification by smoking and other variables in their analyses.

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