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Response to the Review by Fisher and Ma

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Dear Editor

We wish to reply to the review by Fisher and Ma (2012), a critique of our recent report that periodontitis was found to predict elevated C-reactive protein levels in chronic kidney disease published in *Journal of Dental Research*.¹ While we fully share the philosophy that evidence must be evaluated in order to correctly direct science, a number of key assertions in the Fisher and Ma paper merely reflect differences of opinion on choice of methodology and are not examples of fatal flaws invalidating findings.

The authors questioned our classifications of both chronic kidney disease (CKD) and periodontitis status. We defined CKD using a recently developed scheme that combines estimated glomerular filtration rate (eGFR) values <60 ml/min/1.73 m² and albuminuria >30 mg/g, which has been shown to accurately assess risk prediction.² Fisher and Ma attempted a comparison between the CKD frequencies of our study¹ and Coresh et al³ study. However, the populations were selected based on different criteria (e.g. age) and the exposures (e.g. GFR estimation and CKD cutoffs) were defined with different methods. Limitations in these comparisons exist and have been recognized in the past.^{4,5} Nonetheless, the eGFR equation we used is considered valid though, of course, reasonable arguments can be made on both sides about how well it represents CKD.

Regarding the periodontitis status, we selected the American Academy of Periodontology (AAP)/Centers for Disease Control and Prevention (CDC) definition, which has been widely accepted in epidemiological studies and has been adopted in official US public health publications on national prevalence of periodontitis.⁶ Eke et al describe this definition as “conservative based on measurement of probing depth (PD) and clinical attachment loss (CAL) at interproximal sites, ensuring that to the extent subjects designated as cases were in fact cases”.⁷ We also would like to point out that our findings emphasized the importance of the extent of periodontitis (generalized vs. localized) as defined by more than 30% of sites diagnosed with periodontitis. Our results underlined the significant contribution of generalized periodontitis to systemic inflammation. However, in their conclusions Fisher and Ma failed to recognize the difference between “periodontitis prevalence” and “extent of periodontitis”, which were two distinct categorical variables used in our analyses leading to separate results and interpretations.

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Another concern was our characterization of the National Health and Nutrition Examination Survey (NHANES) sample as representative of the U.S. population and our lack of specification about which analytical weights were used. We direct readers to the NHANES website, which states that when weights are applied the findings are considered “representative of the U.S. Census civilian non-institutionalized population.”^{8,9} We are unsure if Fisher and Ma take exception because we did not include the term non-institutionalized when describing representativeness of the sample or if they believe one cannot make any inferences about the general U.S. population from NHANES datasets. Weights were appropriately applied per NHANES guidelines but the specification was removed based on editorial recommendations of the original manuscript. This seems to us a minor journalistic point, and, surprising, given that neither did Fisher et al (2008) specify the NHANES weights in a recent publication.¹¹ Lastly, the C-reactive protein (CRP) cut-point we used was called into question. This value has been used in a number of studies predicting high risk of cardiovascular disease¹⁰ as well as in a recent paper by Fisher et al paper (2008) on periodontitis risk and CKD.¹¹ While analyzing CRP as a continuous value would be preferred, the distribution of CRP values in the NHANES III population is severely skewed and, accordingly, logistic regression models to explore CRP as a dichotomous endpoint are not uncommon.¹²

In closing, the critiques of style (e.g. *t*-tests had been mentioned in the methods section but not reported in results) seem to us to be far afield from the purpose of an evaluation of evidence, and, in our opinion, would be best left to editors and reviewers of the original publishing journal. We also do not believe that evaluation of a single study warrants the sweeping title of the Fisher and Ma review, which implied that the extant scientific evidence to date was judged to be lacking.

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