

Very high risk of bias

Sir, we have appraised the study ‘Oral hygiene, mouthwash usage and cardiovascular mortality during 18.8 years of follow-up’¹ and found its methods to be at ‘very high risk of bias’ according to the ROBINS-E tool,² rendering its findings unreliable.

The main independent variable, oral hygiene self-care (OHS), was measured by self-report. Not only is oral hygiene self-report untrustworthy, the method used (frequency) does not indicate OHS quality. People who report more frequent OHS are more likely to be those who engage in healthier behaviours overall, reducing their overall risk of cardiovascular mortality, thus confounding the observed association. The authors also deviated from their protocol and created three categories of oral hygiene (‘poor’, ‘good’ and ‘better’) instead of the original four, mixing those who never floss with those who floss once a week, which likely inflates any association between OHS and plausible confounders (misclassification bias³). Those who floss once per week are probably very different from those who never floss, but not that different from those who floss more than once per week.

Oral hygiene and covariates were measured only at baseline. Single baseline measurements are poor proxies for long-term behaviours or outcomes, and poor covariate measurement has led to the ‘discovery’ of many spurious risk factors in epidemiology.⁴ To support OHS stability through life, authors cited a study⁵ comparing toothbrushing duration and number of strokes in videos of participants brushing their teeth in the 1970s with videos of a different group of participants brushing their teeth in 2010. This clearly cannot demonstrate stability of OHS frequency in the same individuals.

The authors failed to acknowledge the proportion of participants who ever smoked, had coronary artery disease, hypertension, dyslipidemia and diabetes was higher in the ‘poor’ OHS group at the baseline. This strongly indicates that the study findings are likely influenced by residual confounding.

Conclusions were overly assertive, implying observed associations are causal and free from confounding. The sentences ‘Good OHS significantly lowered the risk of CVD mortality relative to poor OHS’ and ‘Our results have high public health importance because brushing and flossing are relatively inexpensive and have low risk of adverse

effects’ suggest that, as most people brush their teeth at least once daily, if only they started to floss several times per week, their risk of dying from CVD would reduce 50%. This suggestion clearly lacks biological plausibility.

The overall reporting of the study was poor (our evaluation indicated that only half of STROBE⁶ elements have been covered) and it was noticeable the lack of acknowledgement of any existing evidence syntheses to support the need for this study and placing the results in context.

In summary, we have evidenced how this study does not provide reliable evidence that poor OHS causes CVD mortality, as the causal association proposed lacks convincing biological plausibility, and potential confounders have not been well measured nor thoroughly considered in the data analysis. It is crucial that evidence-based dentistry acknowledges the need to better conduct, report, and infer from associative observational studies. Failure to do so may result in our practices being founded on references rather than evidence.⁷

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References

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The authors respond

Sir, we are responding to the letters ‘Yet another cautionary tale?’ by P. Hujuel (doi: [10.1038/s41415-023-5951-1](https://doi.org/10.1038/s41415-023-5951-1)) and ‘Very high risk of bias’ by A. P. Pires dos Santos, P. Nadanovsky and D. Nunan (doi: [10.1038/s41415-023-5949-8](https://doi.org/10.1038/s41415-023-5949-8)).

Both Hujuel and Pires dos Santos *et al*. suggested that our results may be biased due to residual confounding by smoking or health awareness. However, residual confounding can be minimised if the analyses were done correctly and if the investigators made careful adjustments for potential confounding factors.¹ To further refute these criticisms, we conducted a restricted analysis among only never-smokers. The results were quite similar to what we had presented in the current paper,¹ with HR = 0.52 (0.22–1.23), p = 0.14. The non-significant p-value is due to the sample size reduction arising from restriction to never-smokers as we explained in our book chapter.² When we adjusted for the health awareness marker, regular dental check-ups, the results were also similar to the results presented in the current publication: HR = 0.50 (0.29–0.88) p = 0.02. Thus, we are confident that good oral hygiene is driving the CVD mortality risk reduction in our study.¹ Clearly, oral self-care is inversely related to inflammatory markers such as systemic CRP and oral innate immune marker salivary lysozyme levels. But it is not associated with periodontitis or BMI. See Figure 1.

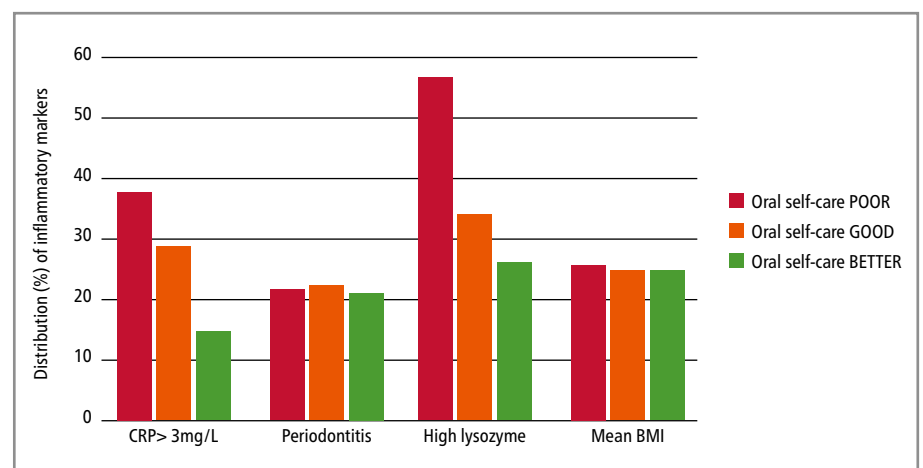


Fig. 1 Oral hygiene self-care and inflammatory markers

Pires dos Santos *et al.* emphasised the limitations of self-reported data. We concur with them, that self-reported data are less reliable. However, oral hygiene self-care does not have any other instrument but self-report. It is unfortunate that these scholars do not recognise the benefits of oral hygiene self-care but only see the deficiencies of self-report. Similarly, physical activities are difficult to assess and especially by self-report.³ However, many studies use the frequency of exercise as a proxy and are accepted as valid.⁴ Now physical activities are recognised as beneficial for health.⁵ The same acceptance should be given to self-reported oral hygiene performance.

We would like to point out to Hujool and Pires dos Santos *et al.* that the risk reduction of 50% is relative to those who did not 'brush or floss'. It is not an absolute risk reduction. A classic example of differences between 'relative risk' and 'absolute risk' can be found in the JUPITER trial for rosuvastatin [see comment⁶]. The CVD event rate in the placebo group was approximately 3% and the same in the statin group was 1.6%, thus, although this trial reported a highly significant relative risk reduction of 44%, the absolute risk reduction was only 1.4%. Per our calculation: $(251/8901 - 142/8901) \times 100 = 1.4\%$.

We would like to offer a word of caution to Hujool who wrote 'a failure to take hormone replacement therapy in post-menopausal women caused cardiovascular disease, that insufficient intake of dietary carotenoids caused cancer, and that periodontitis during pregnancy caused adverse pregnancy outcomes'. These are transposition of reported study results. Even if the relationship is causal, increased or decreased risk is not the same as 'disease' or 'non-disease' occurrence. One should not invert the reported results because 'estrogen replacement therapy decreased the risk of CVD' and 'a failure to take hormone replacement therapy caused cardiovascular disease' are two different events in inverse direction as we have explicated.⁷ We also would like to inform Pires dos Santos *et al.* that the ROBINS-E tool is not universally accepted as useful.⁸ Lastly, we thank *BDJ* and its reviewers for giving us the opportunity to discuss these issues openly and fairly.

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Restorative dentistry Somewhat misleading

Sir, we would like to offer some comments in relation to the interpretation of our published research data,¹ as part of a recent article published in the *BDJ*.² With reference to our investigation reporting on the 5.5-year clinical performance of direct composite resin restorations for the full mouth rehabilitation for patients with severe tooth wear, Dr Hassall has stated that, 'Level 1 and Level 2 failures required repair or replacement, while Level 3 failures (small chips) were polished or accepted. Combined Level 1 and 2 failures were high at 32.5% and if Level 3 failures were included, failure rose to 67.6% after only five years.'

As part of our investigation, there were 676 anterior direct resin composite restorations prescribed for the treatment of tooth wear, observed for a mean period of 62.4 months. Failures were described as, either, a 'Level 1' failure that had a severe deficiency and required replacement of the restoration (to include the need for endodontic treatment or a dental extraction – a catastrophic failure), 'Level 2', a type of failure which referred to the presence of localised deficiencies that were repaired, and 'Level 3' failure, denoting the presence of a small material chip, which would require refurbishment by polishing or needed no further intervention. As part of

the data analysis, the following descriptions were applied; 'Level 1' – a catastrophic failure, 'Level 2-', combined Level 1 and 2 failures and 'Level 3-', all levels of failure observed. In total at the 5.5-year mark, there were 19 Level 1 failures (2.8%), 58 Level 2- failures (8.6%) and 72, Level 3- failures (10.7%). The combined Level 1 and Level 2 failures for the overall anterior restorations were in fact 8.6% (and not 32.5%) and 10.7% (opposed to the quoted 67.6%) for the overall sample, with an overall annual failure rate for all types of failures combined (Level 3-) of approximately 2.2%.

The author of the *BDJ* article has referred to an overall rate of failure that was approximately six times greater than the actual finding. This is somewhat misleading. Whilst significantly higher failure rates were observed where anterior veneer restorations required further visits for completion, based on our overall findings, we concluded that direct resin composite, with proper case planning,³ can offer an acceptable medium-term solution for treating severe generalised tooth wear. This included the prescription of posterior direct resin composite restorations, noting, higher-risk patients were not excluded in our full sample of 1,269 restorations. This contrasts with the author's interpretation of our data, and this is of material relevance. The use of direct resin composite applied in an additive, minimally invasive manner has many benefits for the restorative rehabilitation of tooth wear, to include some documented improvements to patients' oral health-related quality of life post-intervention.

We feel the author is incorrectly using our paper to support his point of view and would kindly request an appropriate erratum to the published paper.

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Dominic C. Hassall responds: The paper considered¹ presents data for all regions of the mouth including the anterior maxilla for one session and two session direct composite veneers on maxillary anterior teeth for advanced tooth wear.

My paper² selected the two session anterior maxillary data as this is the most aesthetically demanding area and it clearly highlights the limitations of traditional composite techniques.

For two session maxillary veneer placement combined level 1, 2 and 3 failure is indeed very