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EDITORIAL

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or more than a century now we have seen • reports either in favour or against a possible association between oral and systemic health. It all started from an old and intriguing hypothesis named the "focal theory", which suggested a causal association between common oral diseases (caries and periodontitis) and various pathological conditions at distant organ sites in the body (ie, heart, kidney or joints).¹ Over the past 10–15 years, however, the evidence provided in support of a positive association between poor oral health and systemic pathologies such as cardiovascular diseases (CVDs) or diabetes has not always been convincing.² It is reasonable to believe that bacteria involved in oral infections, such as periodontitis, might disseminate into the systemic circulation and possibly cause damage either directly at distant sites (ie, endothelial dysfunction) or indirectly by stimulating a systemic metabolic/ inflammatory host response. Our group has recently provided evidence in support of both hypotheses showing an association between successful periodontal treatment and both changes in metabolic/inflammatory markers3 4 and improved endothelial function.5

Despite a wealth of both experimental and clinical data, however, this association seems to be modest and strongly confounded by a series of shared risk factors (age, gender, cigarette smoking, hypertension, diet and obesity) that are common for both oral (caries and periodontitis) and systemic diseases. In particular, there is little doubt about the residual confounding on the association between periodontitis and CVD deriving from cigarette smoking or from the inadequacy of assessing tobacco exposure in past epidemiological research.67 Moreover, interpretation of the data reported is further complicated by the lack of consistency in various reports owing to the use of various screening indices for poor oral health. Although the presence of advanced carious lesions can be easily identified, several investigators have attempted diagnosis of active periodontal disease using a variety of clinical and radiographic measures, not necessarily achieving representation of the "true" disease activity. Among these unreliable oral health indices, information on tooth loss has been repeatedly proved to be easier to collect in clinical trials and less prone to measurement error.8 Indeed edentulousness as a proxy of oral health has already been associated with disease-specific mortality in prospective cohort and case-control studies.9-13 However, the

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information provided by this index is difficult to interpret as tooth loss provides limited information on the possible mechanisms involved that may explain disease aetiology and pathogenesis.

In this issue of the journal, Tu *et al* report an association between tooth loss and increased mortality from CVD in the Glasgow Alumni Cohort (*see article on page 1098*).¹⁴ The research design and methodology adopted in this investigation are unique and well chosen for several reasons. First, participants of the Glasgow Alumni Cohort were examined (including a basic oral health assessment) at an age (20–30 years) when smoking could have had little effect on oral health. This strengthens their conclusions on the positive association between poor oral health as defined by tooth loss and patterns of mortality later in life.

Secondly, Tu *et al* also conducted an additional subgroup analysis in those alumni classified as smokers and non-smokers, showing that cigarette smoking did not present an additive effect on CVD mortality patterns in relation to tooth loss in this cohort.

Third, these findings are further confirmed as Tu *et al* investigated the association between tooth loss and other-causes of mortality (ie, cancer mortality), reporting no substantial associations.

Finally, Tu *et al* suggest that the association between poor oral health and CVD mortality might not be linear. Using an innovative statistical approach, the authors proposed a non-multiplicative association between tooth loss and CVD mortality and therefore posed a new and interesting question: "are there different patterns of association between poor oral health and systemic health outcomes and might this explain the variability in magnitude of the association between poor oral health and systemic outcomes reported in epidemiological research?". This question provides a new perspective on the association between poor oral health and chronic diseases, which should be examined by further research.

Furthermore, Tu *et al* provide evidence for choosing tooth loss as a proxy of oral health, but at the same time their study also demonstrates all the difficulties and limitations in using this particular index when it comes to understanding which mechanisms might link oral health with systemic diseases. Tu *et al* in their study had the advantage that the sample population was quite young and therefore they correctly suggested that caries was likely to be the main reason for tooth loss. However, the lack of information on further tooth loss during the long follow-up of the study does not allow us easily to interpret the association. We are also unable to conclude if tooth loss at

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Editorial

a young age in this cohort was already associated with substantial CVD or if it is a proxy for other underlying conditions. Nevertheless, there is evidence to support the hypothesis of a positive association between poor oral health and both degree of severity and progression of carotid atherosclerosis.¹⁵

As tooth loss causes a change in peoples' diet and nutrition¹⁶ we might speculate that this may affect future risk of coronary or cerebrovascular diseases.¹⁷ Indeed, evidence suggests an important immunomodulatory role of several natural nutrients, and an alteration in nutrition could impact systemic low-grade inflammation and related metabolic/cardiovascular diseases such as diabetes and atherothrombosis.¹⁸

On the other hand, tooth loss is inevitably linked to individual social status.^{19 20} People who have had less access to quality dental care since a young age are those who will be more likely to experience tooth loss. Although Tu *et al* included in their statistical models validated measures of socioeconomic status of study participants, we cannot exclude the possibility of residual confounding by this important factor.

The study by Tu *et al* suggests that tooth loss used as an index for poor oral health is related to CVD mortality, but the complex interplay between biological and social factors involved does not provide us with an explanation for this association. More longitudinal studies with accurate assessments of both oral and systemic health, and randomised controlled clinical trials aimed at health promotion, are warranted.

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