Evidence Summary:
Dietrich, Thomas; Webb, Ian; Stenhouse, Laura; Pttni, Amrit; Ready, Darren; Wanyonyi, Kristina; White, Sandra; Gallagher, Jennifer Elizabeth

DOI:
10.1038/sj.bdj.2017.224

License:
None: All rights reserved

Citation for published version (Harvard):

Link to publication on Research at Birmingham portal

General rights
Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

• Users may freely distribute the URL that is used to identify this publication.
• Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
• Users may use extracts from the document in line with the concept of ‘fair dealing’ under the Copyright, Designs and Patents Act 1988 (?).
• Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy
While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.
Evidence Summary: The relationship between oral and cardiovascular disease

Thomas Dietrich, Ian Webb, Laura Stenhouse, Amit Pattni, Derren Ready, Kristina L Wanyonyi, Sandra White, Jennifer E Gallagher

Professor Thomas Dietrich
Professor and Head of Oral Surgery
The School of Dentistry, University of Birmingham, 5 Mill Pool Way, Edgbaston, Birmingham B5 7EG
Tel: +44-121-4665494
T.Dietrich@bham.ac.uk

Dr Ian Webb
Consultant Cardiologist King's College London
King's College Hospital
Denmark Hill
Bessemer Road
London SE5 9RS
ianwebb@nhs.net

Dr Laura Stenhouse
Specialty Trainee/ACF in Special Care Dentistry
Birmingham Teaching Hospital
Mindelsohn Way
Edgbaston
Birmingham, B15 2TH
laurastenhouse22@googlemail.com

Dr Amit Pattni
STR Oral Surgery
York Hospital
Wigginton Rd
York YO31 8HE
amit.pattni@nhs.net

Dr Darren Ready
Gastrointestinal Bacteria Reference Unit National Infection Service
Public Health England
derren.ready@phe.gov.uk

Dr Kristina L Wanyonyi BDS, MPH, PhD, DDPH.RCS (Eng), FHEA
Dental Public Health Teacher/ Research Associate
Population and Patient Health Division
King’s College London Dental Institute
Denmark Hill Campus
Bessemer Road, SE5 9RS
London
Tel:+44(0)2032994756
Mobile: +447957718679
kristina.wanyonyi@kcl.ac.uk
Dr Sandra White  
Director of Dental Public Health  
Population Health & Care Division  
Health and Wellbeing Directorate  
Public Health England  
Skipton House  
80 London Road  
London SE1 6LH  
Tel: +44 (0) 203 6820911  
Mobile: 07917184998  
sandra.white@phe.gov.uk

Professor Jennifer E Gallagher MBE  
Head of Population and Patient Health  
Newland Pedley Professor of Oral Health Strategy  
Honorary Consultant in Dental Public Health  
King’s College London Dental Institute  
Denmark Hill Campus. Bessemer Road, London SE5 9RS  
Tel: 02032995171/3481  
Admin (research)  
jenny.gallagher@kcl.ac.uk

Corresponding author  
Professor Jennifer E Gallagher MBE  
Head of Population and Patient Health  
Newland Pedley Professor of Oral Health Strategy  
Honorary Consultant in Dental Public Health  
Jenny.gallagher@kcl.ac.uk

Key Words:  
Oral health, general health, stroke, tooth loss, caries, periodontal disease, oral health related quality of life, periodontal therapy, periodontal treatment, oral health promotion, surrogate markers, cardiovascular, cerebrovascular, atherosclerotic cardiovascular disease.
In brief

- There was a firm association between oral health (periodontitis, caries and tooth loss) and atherosclerotic cardiovascular disease (coronary heart disease, stroke, and peripheral vascular disease)
- There was no evidence to support any links between oral health and other forms of cardiovascular disease (i.e., non-atherosclerotic such as hypertension, arrhythmias, and heart failure)
- Periodontal therapy is associated with reductions in surrogate markers of atherosclerotic cardiovascular disease (e.g., endothelial function, inflammatory, and oxidative stress markers)
- Oral health promotion improves oral health-related quality of life measures in stroke patients

Abstract

This paper reports on one review of four rapid reviews undertaken to explore the relationships between oral health and general medical conditions, in order to support teams within Public Health England, health practitioners, and policy makers. This review aimed to explore the most contemporary evidence on whether poor oral health and cardiovascular disease occurs in the same individuals or populations, to outline the nature of the relationship between these two health outcomes and to discuss the implications of any findings for health services and future research. The review was undertaken by a group comprising consultant clinicians from medicine and dentistry, trainees, public health, and academics. The methodology involved a streamlined rapid review process and synthesis of the data. The results identified a number of systematic reviews of low to high quality, which suggests that there is fairly robust evidence that there is an increased risk of atherosclerotic vascular disease [ASVD] among individuals with chronic periodontitis, independent of other established cardiovascular risk factors. And some evidence that the incidence of caries and tooth loss is higher in patients with cardiovascular disease, whilst orofacial pain presents as the sole symptom of stroke in some patients. The findings are discussed in relation to implications for service and future research.
Background

Cardiovascular disease (CVD) is a major cause of morbidity and mortality in the UK, in spite of significant improvements in disease prevention, detection and treatment over recent decades (1). Principle disease categories include (a) atherosclerotic cardiovascular disease (coronary, cerebrovascular and peripheral vascular disease), (b) valvular heart disease, (c) heart failure and cardiomyopathies, (d) arrhythmias, (e) infective and autoimmune conditions (including infective endocarditis), and (f) hypertension.

In 2014, Coronary Heart Disease (CHD) alone was the leading single cause of death in the UK (15% of male and 10% of female deaths), and accounted for up to 1-in-20 inpatient episodes. Cerebrovascular disease (stroke) resulted in approximately 39,000 deaths in 2014, and was the third largest single cause of mortality in the UK (6% of male and 8% of female deaths) (2). Data from NHS England spending for 2014 reveal that expenditure for CVD was in the region of £4.3 billion, with the highest amount (40% or £1.7 billion) arising from ‘unscheduled’ or emergency care (2). According to the Global Burden of Disease study, ischaemic heart disease is the leading cause of disability years of life lost in England (1).

The two most common diseases affecting oral health are dental caries and periodontitis. Dental caries is the localised destruction of susceptible dental hard tissues by acidic by-products from bacterial fermentation of dietary carbohydrates (3). Periodontitis is a chronic inflammatory disease caused by bacterial infection of the supporting tissues around the teeth (4). Approximately half of all adults in the UK are affected by some level of irreversible periodontitis, which increases with age, and almost a third have obvious dental decay (5).

Several direct and indirect mechanisms have been proposed as pathophysiological links between chronic periodontitis and atherosclerotic cardiovascular disease (6). Key concepts include the interplay between periodontal pathogens, vascular endothelial damage and atherogenesis. Systemic inflammation, with chronically elevated inflammatory markers, is common to both disease processes, though to what extent anatomically remote sources of inflammation interact in causative fashion is unclear. Molecular mimicry may additionally play a role, with evidence of cross-reactivity between oral pathogens and both inflammatory and endothelial cell components. Finally, the direct actions of pathogenic bacteria have also been proposed as a potential explanation for the putative relationship between chronic periodontitis and atherosclerotic cardiovascular disease. This has been extensively investigated over recent decades with divergent results, based in no small part due to difficulties in pathogen detection, proof of causal association and challenges in undertaking clinical outcome studies.

This review was limited to synthesising the literature on the primary links between cardiovascular diseases and oral health. This includes the impact of therapeutic interventions to treat oral disease, but not complications that arise from them; acquired infective endocarditis related to oral disease
therapy and cardiac drug-effects (eg gingival hyperplasia in response to dihydropyridines) and their effects on oral health are, therefore, not considered.

Review methods

A rapid review of systematic reviews and/or meta-analyses published between 2005 and 2015 investigating the relationship between cardiovascular disease and oral health was performed. A rapid review involves synthesis of the most current and best evidence to inform decision-makers [13]. It combines elements of systematic reviews with a streamlined approach to summarise available evidence in a timely manner.

Search syntax was developed based on subject knowledge, MESH terms and task group agreements (Figure 1); followed by duplicate systematic title and abstract searches of three electronic databases: Cochrane, PubMed, OVID (Embase, MEDLINE (R), and PsycINFO). Two independent searches were carried out, followed by screening papers by abstract and title for relevance and duplication. Where there was a large body of evidence regarding a particular element, articles were limited to 2010 onwards to reduce the repetition of evidence.

Figure 1

Studies were included if they were either a systematic review and/or meta-analysis and explored a link between cardiovascular disease and oral health. Disagreements between the reviewers and the wider research group were resolved by discussion. Papers were excluded if they were not available in English, did not mention any term related to oral health or cardiovascular disease, full text not available or related to acquired infective endocarditis related to dental intervention, or drug-induced gingival hyperplasia.

The following information was extracted from each paper: author, year, title, journal, population studied, oral disease/intervention, definitions used, methods, comparison/intervention and controls, outcomes, results, authors’ conclusions, quality and quality justification, all shown in the data extraction table.

Table 1

The search identified 247 potentially relevant abstracts, which were screened in duplicate for relevance. Those studies deemed not to have both an oral health and cardiovascular disease component to them were excluded at this stage. The remaining 41 articles were subject to full text review; 23 met the inclusion criteria. A flow diagram of this process is shown in Figure 2.

Figure 2

Quality assessment was undertaken for each systematic review using the PRISMA and AMSTAR tools to ascertain risk of bias. An AMSTAR assessment was carried out on all papers with the methodological quality of the review being rated as “high” with a score between eleven and eight,
“moderate” between seven and four, and “low” between four and zero. The quality of all papers was agreed in group discussion.

Within the themes identified by this review, most of the papers examined the link between atherosclerotic and oral disease, of which 10 examined coronary heart disease and oral disease, and six cerebrovascular disease and oral disease. Of the 22 systematic reviews, 17 were found to be high quality based on AMSTAR tool (6-23), three were of moderate (24-26), and one (27), of low quality. For those with a score below 11, common quality issues were: lack of bias assessment, lack of publication bias assessment, lack of description of methodological rigour and lack of assessment of publication bias. Quality scores, together with the rationale, are presented for each paper in Table 1.

Results: evidence synthesis

The results are synthesised into six sections. Each section combines evidence related to the relationship between a cardiovascular disease to an oral disease or impact of oral disease management.

1) Atherosclerotic cardiovascular disease and periodontitis

A number of systematic reviews of observational epidemiologic studies support an association between periodontal disease and atherosclerotic cardiovascular disease, independent of known confounders (6, 13, 23, 24). Dietrich et al (2013), found this association was stronger in younger compared with older patients, and in males compared with females. There is a limited evidence base for an association between chronic periodontitis and both the risk of recurrent cardiovascular events in patients with established atherosclerotic disease (secondary events) and peripheral vascular disease, respectively (13). There is no evidence to support or refute a causative relationship between cardiovascular disease and oral health (6).

Five systematic reviews with meta-analyses have demonstrated patients with chronic periodontitis have an increased risk of developing coronary heart disease (7, 8, 15, 18, 23). Helfand et al (2009) explored non-traditional cardiovascular risk factors (i.e. those not included within traditional risk models, such as diabetes, blood pressure and cholesterol levels), to explain the risk for incident coronary heart disease (CHD) events in intermediate-risk individuals; chronic periodontitis was one of nine variables studied, but failed conclusively to improve risk prediction (14).

A meta-analysis by Lafon et al. (2014) reported that periodontitis was associated with increased risk of stroke [relative risk 1.63 (1.25, 2.00)] (16). Sfyroeras et al (2012), also suggest an association between periodontitis and haemorrhagic stroke; this association was stronger in males, obese patients and non-diabetics (21).

In summary, the evidence suggests that the incidence of atherosclerotic cardiovascular disease is higher in patients with periodontitis compared to those without.
Atherosclerotic cardiovascular disease and tooth loss

Four systematic reviews (14-16, 20) suggest that tooth loss is associated with an increased risk of cardiovascular disease, in particular the risk of coronary heart disease and stroke, as outlined below.

a) Coronary heart disease and tooth loss

Humphrey et al 2008 (15) pooled estimates, demonstrating that individuals with 0-10 teeth had a relative risk of coronary heart disease and coronary death of 1.34 (95% CI 1.10-1.63) compared to patients with 25-32 teeth (p=0.02). A later meta-analysis by Helfand et al in 2009 (14) likewise demonstrated a 1.34 relative risk (CI, 1.10-1.63) of general cardiovascular disease for persons with 0-10 teeth compared to those with >10 teeth.

b) Cerebrovascular disease stroke and tooth loss

A meta-analysis by Lafon et al., 2014 (16) indicated a pooled risk estimate of 1.39 (1.13, 1.65) when ischaemic and both ischaemic and haemorrhagic strokes were considered together for edentulous patients compared with dentate patients.

c) Circulatory mortality and tooth loss

Polzer et al., (2012) (20) reported that 12 out of 15 studies showed an increased risk of all-cause mortality among individuals with high numbers of missing teeth; seven out of nine studies demonstrated increased circulatory mortality (defined as a primary cardiac cause) in this group.

In summary, although the cause of tooth loss is unclear, the evidence suggests that patients with fewer teeth are more likely to suffer cardiovascular disease and cardiovascular-related death.

III] Stroke and oral health related quality of life

The systematic review by Dai et al 2015 highlights that stroke patients have poorer oral health-related quality of life and oral function (11). It is unclear whether this represents disease association or simply a manifestation of reduced dexterity.

In summary, oral health-related quality of life of stroke patients is significantly worse than those who have not suffered stroke.

IV] Cardiovascular disease and caries/endodontic disease

A systematic review by Dai et al (10), found that patients with stroke have significantly higher caries prevalence [DMFT] scores than healthy controls (10). An earlier systematic review of moderate quality evaluated the potential association between apical periodontitis/endodontic disease and CVD, but found scarce evidence to support this link (27).

In summary, there is some evidence that dental caries and disease associated with infections from dental caries or periodontal tissues are associated with incidence of cardiovascular disease.
**V] Stroke and oral health promotion**

Two systematic reviews (9, 26), of which one was a Cochrane review (9), show that use of oral health promotion could improve oral health of stroke patients. This includes, periodontal therapy or prophylactic extractions and particularly health care training on oral health promotion.

In summary, for patients who have suffered a stroke, oral health promotion can have a significant impact on their oral health.

**VI] Cardiovascular disease and periodontal treatment**

Periodontal treatment has been shown to have the following effects on surrogate markers implicated in cardiovascular disease: reduction in levels of C-reactive protein (12, 19, 22, 25), improvement in endothelial function (6, 12), and reduction in carotid intima-medial thickness (c-IMT) (23). D’Aiuto et al. (2013) reported moderate evidence of a negligible effect of periodontal therapy in reducing interleukin-6 and lipid levels, and limited evidence on the effects on the following surrogates: arterial blood pressure, leucocyte counts, fibrinogen, tissue necrosis factor-α, sE-selectin, von Willebrand factors, d-dimers, matrix metalloproteinase, oxidative stress and CVD events. There was no evidence on the effects of periodontal therapy on subclinical atherosclerosis, serum levels of CD40 ligand, serum amyloid A and monocyte chemo attractant protein.

Although periodontal interventions result in a reduction of certain surrogate markers, there is no evidence that this is associated with changes in atherogenesis or disease outcomes (6). This is supported by Li et al., 2014, who suggest that there is insufficient evidence that periodontal therapy can impact on recurrence of coronary heart disease (17).

In summary, there is a large body of evidence suggesting that periodontal therapy has a significant effect on a number of surrogate markers implicated in cardiovascular disease; however, there is insufficient evidence that periodontal therapy has an impact on recurrence or secondary events of coronary heart disease.

**Summary**

There is high quality evidence to support an association between cardiovascular disease and oral health. This evidence mainly is related to the association between chronic periodontitis and atherosclerotic heart disease and is independent of confounding factors as drawn from epidemiological observational studies. Notably, no causal relationship has been established between cardiovascular disease and periodontal disease and (6), and the results suggest associations of varied strength between other oral diseases such as caries and oral facial pain and cardiovascular disease.

This review was limited by the widespread discrepancy in the definitions of cardiovascular and chronic periodontitis used in the literature. Kelly et al in 2013 had similarly highlighted significant structural and methodological variability among the published systematic reviews and meta-analyses regarding
the connection between periodontitis and CHD (28). A strength of this review is the high number of meta-analyses. Furthermore, the focus on a wide range of cardiovascular and oral disease provides a wider range of evidence identifying areas of interest that may require further research.

The findings in this review have significant implications for health services and research. In relation to health services generally, healthcare professionals diagnosing and managing oral and cardiovascular disease should be aware of the associations highlighted in this review and the implications for patient care and health outcomes. A concerted effort is necessary across disciplines to ensure relevant cross-referrals and risk assessments in order to reduce the incidence and improve prognosis of these diseases.

Dental professionals should provide health promotion advice and signposting for patients presenting with chronic periodontitis in the presence of other cardiovascular disease risk factors such as obesity, diabetes and increased age. For example, the NHS Health Check has been introduced for people aged 40-74 to focus on the principle behavioural and physiological risk factors for CVD. Dental professionals should encourage uptake of this service for those considered at increased risk of CVD.

Quality of life of patients who have suffered stroke is significantly altered and the implication of changes in dexterity and oral muscular function can cause further challenges. A daily regime of care should be instituted to maintain oral health and activities to support carers in this role will also be helpful (11).

There is room for well-designed longitudinal studies which can further examine the associations between these two diseases and surrogate markers of disease. It is only following this that firm recommendations can be made with regards to whether further interventions are required. Therefore, observational studies should evaluate the association between periodontitis and adverse events in high-risk populations. Randomised controlled trials are required to establish the effectiveness of periodontal treatment in high risk groups on surrogate cardiovascular endpoints.

**Table 2**

In summary, there is a firm association between oral health (periodontitis, caries and tooth loss) and atherosclerotic cardiovascular disease; that is coronary heart disease, stroke, peripheral vascular disease. There is little or no evidence to support any links between oral health and other forms of cardiovascular disease that is non-atherosclerotic such as hypertension, arrhythmias and heart failure. Periodontal therapy is associated with reductions in surrogate markers of atherosclerotic cardiovascular disease such as endothelial function, inflammatory and oxidative stress markers. There is evidence that oral health promotion interventions, involving staff and patients, improve oral health-related quality of life measures in stroke patients.

**Acknowledgements**
We would like to acknowledge the support of Dr Francesco D’Aiuto of University College London on this paper and during workshops. We would like to acknowledge the support of Public Health England, the Royal College of Surgeons and the British Dental Association.
Bibliography