

# Periodontal diseases and health: Consensus Report of the Sixth European Workshop on Periodontology

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Kinane D, Bouchard P. Periodontal diseases and health: Consensus Report of the Sixth European Workshop on Periodontology. J Clin Periodontol 2008; 35 (Suppl. 8): 333–337. doi: 10.1111/j.1600-051X.2008.01278.x.

## Abstract

**Introduction:** The remit of this group was to update the knowledge base on periodontal diseases and health.

**Material and Methods:** The literature was systematically searched and critically reviewed in five specific topics.

**Results: Prevalence of periodontitis:** The data suggest a trend towards a lower prevalence of periodontitis in recent years.

**Adverse pregnancy outcome:** The findings indicate a likely association between periodontal disease and an increased risk of adverse pregnancy outcomes. There is no evidence that treating periodontal disease decreases the rate of adverse pregnancy outcomes.

**Prevalence and distribution of periodontal pathogens:** Genetic analysis of bacteria has demonstrated an unanticipated diversity within species. Carriage rates and particular subsets of these species vary between ethnic groups. Few of these differences can be related to differences in disease prevalence.

**Diabetes mellitus:** Evidence on the association supports the concept of increased severity but not extent of periodontitis in subjects with poorly controlled diabetes. It is inconclusive that periodontal treatment results in improved metabolic control.

**Cardiovascular diseases:** Evidence suggests that having periodontitis contributes to the total infectious and inflammation burden and may contribute to cardiovascular events and stroke in susceptible subjects. The impact of periodontal therapy must be further investigated.

Key words: cardiovascular; diabetes mellitus; periodontitis; preterm birth; prevalence

Accepted for publication 20 May 2008

## Conflict of interest and source of funding statement

Group E participants declare that they had no conflict of interests.

The 6<sup>th</sup> European Workshop has been financially supported by an unrestricted educational grant from Straumann AG. The sponsor had no impact on the program or on the deliberations of the European Workshop.

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The remit of this working group was to update the existing knowledge base on the impact of periodontal disease on health. Several published systematic reviews from the 4th EAP Workshop formed the starting point for this update, and in addition, specific innovations not covered in previous workshops were included. For this purpose, the literature was systematically searched and critically reviewed.

Five manuscripts were produced on specific topics identified as areas where advances in knowledge had been made in periodontal and general health and which were deemed to be potentially important in the future clinical practice.

- Has the prevalence of advanced periodontitis changed in Europe during the last 30 years?
- A critical assessment of adverse pregnancy outcome and periodontal disease.
- Prevalence and distribution of major periodontal pathogens worldwide.
- Effects of diabetes mellitus on periodontal and peri-implant conditions. Update on associations and risks.
- Cardiovascular and periodontal disease. An update on the associations and risks.

Although the purpose was to produce systematic reviews with meta-analyses in all five manuscripts, the paucity and heterogeneity of the available clinical research in some specific areas precluded this approach and favoured a more narrative approach.

Themes common to all of the reviewed topics emerged, which were deemed fundamentally important to the accurate interpretation of study design, outcomes, interpretations and future research. Among these we have identified the following.

Causal inference is established *incrementally* through a synthesis of data stemming from different types of studies. Epidemiologic studies (case-control, cross-sectional and prospective cohort studies) are usually the first to generate association data between putative risk factors (exposures) and adverse health outcomes. Initially observed univariate associations are subsequently examined in multivariate settings to adjust for potential confounders. Factors identified as independent exposures are examined in additional studies to dissect biologi-

cally plausible pathways by which these effects may be mediated. These studies may span a broad spectrum of approaches including *in vitro* studies, *in vivo* mechanistic experimental animal studies, human observational, prospective cohort studies and intervention trials focusing on specific biomarkers. Ultimately, randomized controlled clinical trials (RCTs) examine the effect of specific interventions (with respect to time point, mode of administration, intensity, etc.) on particular *clinical* outcomes or on validated and widely accepted surrogate markers.

Clinical trials with a statistically significant positive outcome are easy to interpret and indicate that the tested intervention is effective in favourably altering the adverse health outcome. If independently corroborated by additional clinical trials, their findings are interpreted as the ultimate proof that the exposure was causative of the condition. However, clinical trials with non-significant outcomes are far more difficult to interpret. In situations where there are wide confidence intervals, the direction of the effect cannot be determined with adequate precision, thus the findings are inconclusive.

Repeated, independently carried out, negative clinical trials may ultimately point to the conclusion that the particular adverse health outcome may not be positively modulated by means of the specific intervention. Still, these studies do NOT provide proof that there is a lack of a causal relationship between the exposure and the outcome. Interventions may fail to have an effect on the outcome under investigation due to a variety of reasons such as inappropriate timing, inability to alter the exposure to a sufficient extent and inadequate compliance.

RCTs are ideally suited to assess the effectiveness of the intervention on a disease outcome, change clinical practice, and to inform public health policy. They do not serve as a sole basis for determining causality.

#### **Has the Prevalence of Periodontitis Changed During the Last 30 Years? (Hugosson & Norderyd 2008)**

##### **Conclusions**

This paper reviews global trends in the change in prevalence of periodontitis over the last 30 years. The epidemiology of periodontal disease is briefly reviewed together with the current classification system and the clinical and radiographic

diagnostic methodology in periodontal disease. This review identifies the very limited number of studies that provide prevalence data over time, and this data is discussed in comparison with those stemming from a few corresponding studies from countries outside Europe. The data indicate a possible trend of a lower prevalence of periodontitis in recent years.

##### **Consensus statements**

Limited data from selected populations in Europe and the US points to a decrease in the prevalence of periodontal diseases. These decreases are primarily in gingivitis and mild/moderate periodontitis. The single study that allows a comparison over time of the most severe forms of periodontitis demonstrates no change in prevalence. However, this observation is confounded primarily by tooth loss and a definitive statement on changes in prevalence of severe periodontitis over time is not possible.

##### **Implications for practice**

Precise estimates of prevalence trends over time are essential for the determination of treatment needs, the identification of the determinants of change in prevalence, and subsequent cost-effectiveness analyses to appropriately allocate oral health care resources in order to achieve maximal benefit for the population.

##### **Implications for research**

There is a need for additional studies using well-defined criteria that reflect extent and severity across the entire range of periodontal conditions, so that the trends in prevalence can be defined with precision. Assessment of periodontal status should incorporate an evaluation of dental status parallel to assessments of inflammatory periodontal conditions as well as a documentation of possible changes in established risk factors.

#### **A Critical Assessment of Adverse Pregnancy Outcome and Periodontal Disease (Wimmer & Pihlstrom 2008)**

##### **Conclusions**

Despite wide efforts in the areas of prevention, diagnosis and therapy, the incidence of preterm birth in most of the countries has not reduced. Infections are considered to be one of the important causes. Recently, oral infections have

attracted increasing interest. The objective was to review the evidence for the association and risks between preterm low birth weight deliveries and periodontal diseases as well as the impact of periodontal therapy on pregnancy outcomes. In order to identify studies for this topic, a search in computerized databases up to October 2007 was conducted. The search was limited to clinical human studies published in English. All levels of available evidence were included. There was a clear heterogeneity between the studies, concerning the definitions used for periodontal disease measurement and for adverse pregnancy outcomes. In many papers, there was a remarkable lack of adequate analysis for confounders, making it barely possible to draw any solid conclusions. Although the findings indicate a likely association between periodontal disease and an increased risk of adverse pregnancy outcomes, there is no conclusive evidence that treating periodontal disease improves the rate of positive birth outcomes. It is recommended that further studies including larger cohorts and interventional trials, which clearly define outcome and exposure measures and which adequately control for other confounders, be conducted.

#### Consensus statements

In certain study samples, periodontal disease has been associated with adverse pregnancy outcome(s); this association has not been shown in other populations. There is considerable heterogeneity and inconsistency in periodontal disease exposure definitions among studies of periodontal disease and adverse pregnancy outcome(s). There is considerable heterogeneity in adverse pregnancy outcomes reported in studies of periodontal disease and adverse pregnancy outcome(s), for example: preterm birth, low birth weight, preterm birth and/or low birth weight, foetal growth restriction, stillbirth, pre-eclampsia, and late miscarriage.

There is no consistent evidence that treatment of periodontal disease improves pregnancy outcome(s) across populations.

#### Implications for practice

There is evidence that mechanical periodontal therapy administered in the second trimester is safe and does not have any adverse maternal or infant effects.

Existing evidence from a relatively small, single-centre RCT has shown no advantage in use of adjunctive antimicrobial periodontal therapy to reduce adverse pregnancy outcomes.

#### Implications for research

Future observational and intervention studies should clearly define adverse pregnancy outcomes. For example, preterm birth and low birth weight should not be combined into one outcome variable.

Future observational and intervention studies should clearly define periodontal disease exposure in terms of extent and severity of periodontal disease.

Large sample prospective cohort studies in various populations are needed in order to determine whether and which type of periodontal diseases may have a causative role in adverse pregnancy outcome(s) and whether this role varies among different populations.

If large, prospective cohort studies establish a temporal relationship between maternal periodontal disease *before* or *during* pregnancy and adverse pregnancy outcome(s), large sample, multi-centre RCTs will be needed to determine if appropriately timed and delivered periodontal interventions decrease adverse pregnancy outcome(s) in these populations.

#### Prevalence and Distribution of Principal Periodontal Pathogens Worldwide (Rylev & Kilian 2008)

##### Conclusions

Detailed genetic analysis of bacteria has demonstrated an unanticipated genetic diversity within species, which often reveals evolutionary lineages that are disproportionately associated with infection. There is evidence that some evolutionary lineages of bacteria have adapted to particular ethnic groups. This review analyses to what extent the observed differences in periodontal disease prevalence among ethnically or geographically distinct populations may be explained by restricted host adaptation of clones of principal periodontal pathogens. Carriage rates of several putative periodontal pathogens and particular subsets of these species vary between ethnic groups.

Few of these differences can, with the limited information available, be directly related to differences in perio-

odontal disease prevalence. Asian populations are regularly colonized with *Aggregatibacter actinomycetemcomitans* serotype c with questionable pathogenic potential. Conversely, the JP2 clone of *A. actinomycetemcomitans* has enhanced virulence and causes significantly higher prevalence of aggressive periodontitis in adolescents whose descent can be traced back to the Mediterranean and western parts of Africa. Some genetically distinct types of *Porphyromonas gingivalis* are more associated with disease than others, but additional work is required to relate this to clinical differences.

Studies that take into account differences linked to the genetics of both patients and potential pathogens are likely to give better insight into the aetiology of periodontal diseases.

#### Consensus statements

Current evidence indicates that carriage rates of the periodontal pathogens *A. actinomycetemcomitans* and *P. gingivalis* vary between ethnic groups.

Some of these differences may be explained by differences in oral hygiene, local patterns of antibiotic usage and other environmental factors. Other differences seem to be related to host tropism resulting from long-term co-evolution rather than to differences in geography and limited dissemination. Few of these differences can, with the current information, be directly related to differences in periodontal disease prevalence. The only well-documented exception is the JP2 clone of *A. actinomycetemcomitans*, which has distinctly enhanced virulence and causes a significantly higher prevalence of aggressive periodontitis in adolescents whose descent can be traced back to the Mediterranean and western parts of Africa.

Comprehensive genetic studies of bacteria associated with humans reveal striking differences in the pathogenic potential of members of the same species. Recent information indicates that this applies to *A. actinomycetemcomitans*. There is strong evidence from longitudinal cohort studies that the highly toxic JP2 clone of *A. actinomycetemcomitans* has unique pathogenic potential and is associated with initiation of aggressive periodontal disease. Only individuals whose descent can be traced back to the Mediterranean and western parts of Africa are susceptible to infection with the JP2 clone, a fact

that conceivably explains the observed high prevalence of aggressive periodontitis in African Americans, Arabs, Berbers and individuals of Northwest African descent, e.g. in Brazil.

Conversely, the high prevalence of *A. actinomycetemcomitans* serotype c in Asian populations without pronounced periodontitis suggests that at least in this population some members of this serotype are non-pathogenic. More detailed microbiological and prospective cohort studies are required to associate particular subsets of other bacteria with disease, health or particular ethnic groups.

#### Implications for practice

Knowledge of this phenomenon may impact on the diagnosis and treatment of particular ethnic groups.

#### Implications for research

As yet, we have no knowledge of the host determinants of this bacterial tropism. Intervention studies are needed to further assess the clinical effects of lowering the level or eliminating the JP2 clone through treatment. Although the JP2 clone confers high risk for aggressive periodontitis, some non-JP2 clones also confer risk and their contribution should be elucidated. In future, we should test for various clones and determine strategies for preventing aggressive periodontitis, e.g., eradication or other means.

#### Effects of Diabetes Mellitus on Periodontal and Peri-Implant Conditions. Update on Associations and Risks (Salvi et al. 2008)

##### Conclusions

Diabetes mellitus and periodontal disease represent common chronic diseases that may have reciprocal influence. The objective was to review the evidence for the association between diabetes and periodontal disease and the impact of periodontal therapy on diabetic status. A search of MEDLINE-PubMed was performed up to and including December 2007. The search was limited to clinical studies published in English. Publications on animal studies were excluded. The selection criteria included all levels of available evidence: systematic reviews, RCTs, controlled clinical trials, prospective and retrospective cohort studies and case reports.

Available evidence on the association between diabetes and periodontitis supports the concept of increased severity but not extent of periodontitis in subjects with poorly controlled diabetes. Subjects with controlled diabetes do not show an increase in the extent and severity of periodontitis. Studies have demonstrated that periodontitis is associated with poor metabolic control and diabetes-related complications. It is inconclusive that periodontal treatment results in improvements of metabolic control and of markers of systemic inflammation. No evidence is available that improvement of metabolic control in diabetic subjects results in improved periodontal conditions in diabetic subjects with periodontitis. Poorly controlled diabetes may be considered a risk factor for increased severity of periodontal disease. The effects of periodontal therapy on diabetic control and systemic inflammation are not proven beyond doubt and need to be confirmed in large-scale RCTs.

#### Consensus statements

Diabetes and periodontitis represent common chronic diseases that may have reciprocal influence. Interpretation of the available literature is hampered by changing definitions of glycaemic control and the prevalence and management of both diseases.

In terms of diabetes influencing periodontitis, available evidence on the association between diabetes and periodontitis supports the concept of increased severity of periodontitis in subjects with diabetes. Periodontal disease in diabetes subjects is associated with age of onset, duration of diabetes, poor metabolic control and diabetes-related complications. Subjects with controlled diabetes show periodontal conditions comparable to those of the general population. Non-surgical and surgical periodontal therapies are equally efficacious in diabetes subjects with good glycaemic control compared with non-diabetes subjects.

In terms of periodontitis influencing diabetes, subjects with type I and type II diabetes (Pima Indians) with severe periodontitis have more diabetic complications than diabetes subjects with no periodontitis. It is inconclusive whether periodontal treatment results in improvements in metabolic control and markers of systemic inflammation.

#### Implications for practice

The clinician should be aware of the bidirectional relationship between diabetes and periodontal disease and its clinical ramifications for diagnosis and treatment.

There is evidence that opportunistic screening for type II diabetes is effective in the dental office, and thus oral care providers may play a role in the detection of undiagnosed diabetes.

#### Implications for research

The effects of different modalities of periodontal therapy on glycaemic control need to be addressed in appropriately powered and designed intervention studies.

Additional studies should address the association of periodontitis with the metabolic syndrome (a precursor of type II diabetes) and with gestational diabetes.

The effects of diabetes on implant therapy and regenerative therapy should be addressed in appropriately powered and designed intervention studies.

#### Cardiovascular and Periodontitis. Update on the Associations and Risk (Persson & Persson 2008)

##### Conclusions

Associations between periodontitis and cardiovascular diseases (CVDs) have been recognized. A literature review since the previous European Workshop on Periodontology has been conducted. The lack of reliable epidemiological data on disease prevalence makes it difficult to assess the associations and risks between periodontitis and CVD. Data based on meta-analysis have suggested odds ratios between 1.1 and 2.2. The impact of periodontitis on serum markers of inflammation such as CRP, interleukin-6, plasminogen factors, white blood cell counts, and on serum lipids, brachial artery flow rate, intima media thickness suggest that having periodontitis has a negative impact on such CVD surrogates. There is evidence that within 6 months following periodontal therapy, brachial artery flow rates improve. Following intensive periodontal therapy, however, serum high-sensitivity CRP values increase, whereas brachial artery flow rate may temporarily decrease, suggesting that medical consults before periodontal treatment of subjects at high risk for

acute coronary syndrome or stroke should be performed. Tooth eradication may also reduce the systemic inflammatory burden. Preventive periodontal care may be the most important effort in reducing the risk for CVD by maintaining healthy oral conditions.

Available evidence suggests that having periodontitis contributes to the total infectious and inflammation burden and may contribute to cardiovascular events and stroke in susceptible subjects.

The impact of periodontal therapy must be further investigated.

#### Consensus statements

Since the last similar systematic review (4th EWP), a consistent positive but weak association has been reported between periodontitis and increased future risk of cardiovascular events (MI, stroke). One meta-analysis reported an odds ratio between 1.14 (CI 1.01–1.2) in prospective studies and 2.2 (CI 1.6–3.1) in case controls and the second meta-analysis 1.6 (CI 1.3–1.9).

There have been attempts to better define periodontitis as an exposure in relation to atherosclerosis. There is inconsistency, however, in the definition of periodontitis in epidemiologic research. There is evidence that periodontitis is associated both with endothelial dysfunction and with validated measures of sub-clinical carotid atherosclerosis (intima media thickness: IMT), which correlate with future cardiovascu-

lar events. Data suggest that periodontitis elicits low-grade systemic inflammation. There is modest evidence to suggest that periodontal therapy lowers levels of serum CRP; however, this finding is not consistent across other biomarkers.

There is evidence that periodontal therapy improves measures of endothelial function (endothelial dysfunction is a very early marker of vascular disease).

There are still no published trials assessing the impact of periodontal therapy on the incidence of cardiovascular events.

#### Implications for practice

The clinician should be aware of the potential relationship between CVD and periodontal disease and its clinical ramifications in periodontal management.

#### Implications for research

As suggested in the last EWP, prospective multicentre cohort studies in different countries should be performed to ascertain the etiological role of periodontal diseases in atherosclerosis and CVD events (MI and stroke). There is a need in these studies to use standardized tools in assessing periodontitis as an exposure both with clinical, microbiological and immunological measures. Particular emphasis should be devoted to understand the role of confounders and effect modifiers in the association between these two diseases. In addition, studies are needed to elucidate biologi-

cal mechanisms whereby periodontal disease can mediate the risk for atherosclerosis and CVD events.

We need properly designed studies assessing the immediate and long-term impact of periodontal therapy on cardiovascular events or validated surrogate markers of cardiovascular events. Well-designed prospective cohort studies may inform the design of large multicentred RCTs to investigate the possible effect of periodontal therapy on CVD. The use of validated surrogate markers for CVD would enhance the efficiency and cost-effectiveness of such RCTs.

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