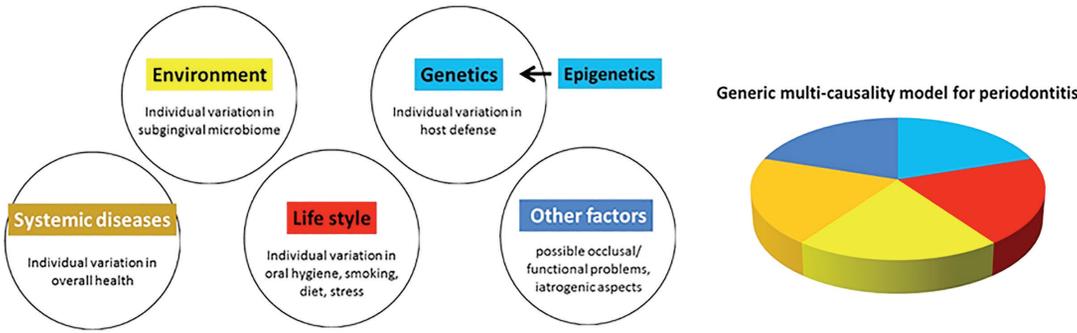


DEBATE EXPERT VIEW FOCUS RESEARCH Editor: Joanna Kamma

# What is the extent of the role played by genetic factors in periodontitis?



While genetic factors are known to play a role in periodontitis, a lot of research still needs to be done to understand the mechanisms that are involved. Indeed, the limited extent to which the genetic factors associated with periodontitis have been identified is “somewhat disappointing”, say Bruno G. Loos and Deon P.M. Chin, from the Academic Centre for Dentistry in Amsterdam.

In a comprehensive overview of current knowledge, they outline what is known today and discuss the most promising lines for future inquiry. They note that the phenotypes of aggressive periodontitis (AgP) and chronic periodontitis (CP) may not be as distinct as previously assumed because they share genetic and other risk factors.

More on pages 2-5



## Discover latest JCP research

The *Journal of Clinical Periodontology* (JCP) is the official scientific publication of the European Federation of Periodontology (EFP). It publishes research relating to periodontal and peri-implant diseases and their treatment. The six JCP articles summarised in this edition of *Perio Insight* cover:

- (1) how periodontitis changes renal structures by oxidative stress and lipid peroxidation;
  - (2) gingivitis and lifestyle influences on high-sensitivity C-reactive protein and interleukin 6 in adolescents;
  - (3) the long-term efficacy of periodontal regenerative therapies;
  - (4) tooth loss in generalised aggressive periodontitis;
  - (5) the association between diabetes mellitus/hyperglycaemia and peri-implant diseases;
  - (6) the efficacy of collagen matrix seal and collagen sponge on ridge preservation in combination with bone allograft.
- Edited by Maurizio Tonetti, the JCP is published monthly and has an impact factor of 3.477.

More on page 7-8

## Researchers call for global action on periodontal disease

A call for global action to reduce the impact of periodontal diseases on health and well-being has been issued in a health-policy paper published in the *Journal of Clinical Periodontology* (JCP), the EFP's scientific journal.

The paper has been endorsed or supported the EFP and 50 other international and national societies of periodontology.

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# What is the extent of the role played by genetic factors in the aetiology of periodontitis?

By Bruno G. Loos and Deon P.M. Chin.

While genetic factors are known to play a role in periodontitis, a lot of research still needs to be done to understand the precise mechanisms involved. Indeed, the limited extent to which the genetic factors associated with periodontitis have been identified is somewhat disappointing, although there are some promising lines of inquiry.

Periodontitis is a complex chronic inflammatory disease, in which there are multiple causal components<sup>1</sup> that play their aetiological roles simultaneously and interact with each other.

At least five domains of causal risk factors can be distinguished for periodontitis (see Fig. 1):

1. Environmental factors (a dysbiotic subgingival bacterial biofilm);
2. Genetic risk factors;
3. Lifestyle factors such as smoking, poor diet, and stress;
4. Systemic diseases, such as diabetes;
5. Other factors, as yet unknown but most likely also including tooth-related, occlusal, and iatrogenic factors.

Within the domain of genetic risk factors for periodontitis, not only do certain genetic variations play a role, *epigenetic* changes in DNA are also involved.

For the last 20 years, the periodontal community has followed the classification of two distinct phenotypes of periodontitis: aggressive periodontitis (AgP) and chronic periodontitis (CP). AgP occurs most often at a younger age (up to 35 years old) and these cases involve more genetic risk factors than CP cases (see Fig. 2).

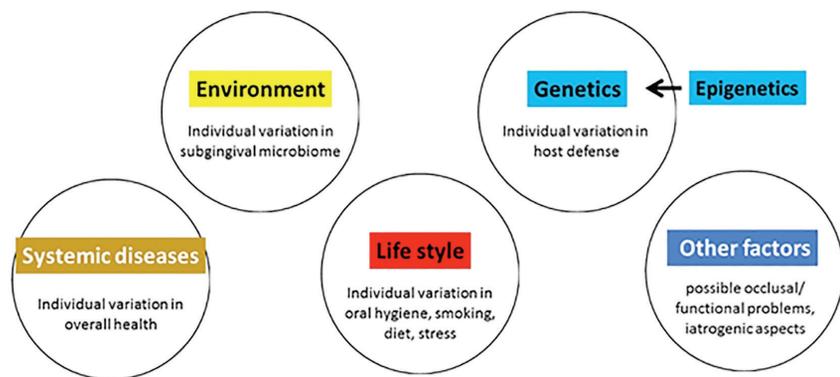
However, the phenotypes AgP and CP may not be as distinct as previously assumed and thus may not really be separate entities, because they do share genetic and other risk factors. It has been long recognised that cases of AgP can occur also in people aged over 35 and that cases of CP can occur in those below this age.

Nonetheless, almost all current studies on genetics use the defined disease entities: either AgP or CP. This has helped researchers to focus on well-described case-control studies, something that is much needed in the search for genetic risk factors.<sup>2</sup>

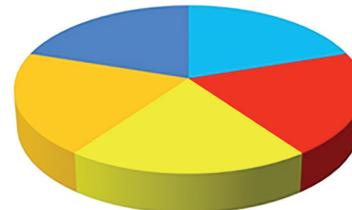
## Genetic basis of periodontitis

On the basis of epidemiological studies of twins and families with a higher rate of AgP, it can be concluded that in the younger patients the genetic contribution may account for as much as 50% of causal factors, while in the older patients a genetic contribution of at most 25% has been estimated.<sup>3</sup>

Fig. 1. Genetic multi-causality model for periodontitis



Generic multi-causality model for periodontitis



**Note: The multicausality model for periodontitis. Causal factors are ordered in five domains and they play a role simultaneously, as well as interact with each other. Importantly, the relative contribution of each causal factor varies among patients, therefore the size of each “piece” of the pie chart should be estimated per individual patient.**

See: Loos, B. G., Papantonopoulos, G., Jepsen, S. & Laine, M.L. (2015). What is the contribution of genetics to periodontal risk? *Dental Clinics of North America*, 59, 761-780.

As in other complex chronic diseases, it is important to realise that a multitude of genetic variations (probably more than a hundred) are involved, so periodontal disease is called polygenic.

Taking this into account, it is somewhat disappointing that, in the case of periodontitis, the genetic factors associated with or contributing to the pathogenesis have been identified only to a very limited extent and have been poorly validated.

It is also possible that genetic variants associated with periodontitis in, for example, Caucasians may not be associated with other ethnic populations such as Asians, Brazilians, and Africans. While a considerable overlap of genetic variants between different ethnicities is expected, it is important to realise that there will also be population-specific variants of risk genes.

The most common genetic variation between individuals is called a single nucleotide polymorphism (SNP). The frequency of a SNP is on average one per 300 nucleotides.

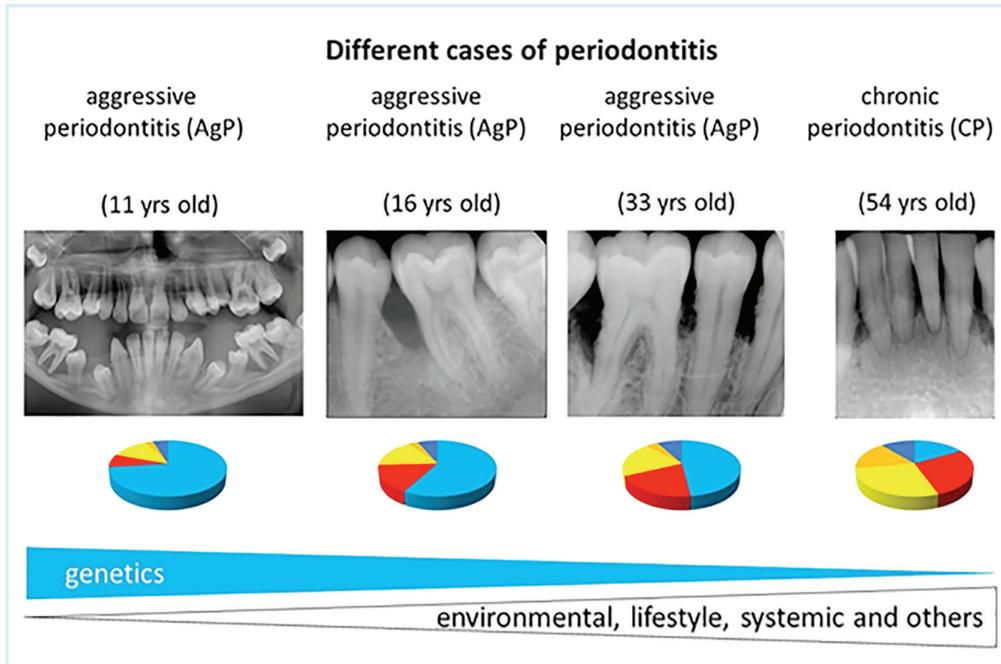
Therefore, it is estimated that there are over 10 million SNPs in the human genome. These are annotated in the haplotype map (HapMap).

There are different types of SNPs: noncoding, coding, and regulatory polymorphisms. In addition, there are other genetic variations such as variable number tandem repeats (VNTR), nucleotide insertions and nucleotide deletions.

Variants in 38 genes have been associated with periodontitis, identified by using either the candidate-gene approach or by genome-wide association studies (GWAS) (see Table 1).

## EXPERT VIEW

**Fig. 2. Genetic contribution to the aetiology of periodontitis**



**Note:** The genetic contribution to the aetiology of periodontitis in relatively younger individuals with aggressive periodontitis has been considered higher than in older individuals with chronic periodontitis. In older individuals, environmental factors (a dysbiotic subgingival bacterial biofilm), lifestyle factors, systemic disease, age (immune senescence) contribute more to periodontitis development, whereas genetic factors play a smaller role.

See: Loos, B. G., Papantonopoulos, G., Jepsen, S. & Laine, M.L. (2015). What is the contribution of genetics to periodontal risk? *Dental Clinics of North America*, 59, 761-780.

### Candidate-gene approach

Most often, the genetic loci, and the genetic polymorphisms that are positioned within these loci, have been chosen for candidate-gene studies of periodontitis based on their perceived participation in various adaptive and innate immune responses. They may also have previously been associated with other chronic inflammatory diseases, such as Crohn's disease, rheumatoid arthritis, and cardiovascular disease. The overlap of the risk genes in chronic diseases is called pleiotropy.<sup>4</sup>

Within the candidate-gene studies, the allele frequencies of selected SNPs are compared between a group of periodontitis cases and periodontitis-healthy controls. Whether a genetic variant has a clinical effect and an effect on the phenotype depends on whether the SNP is located in the coding, non-coding, or regulatory region of the gene. Most genetic risk variants do not result in obvious phenotypic changes, while some may result in clear alterations to function or protein structure.

Many candidate-gene studies that have been performed in periodontitis have had varying and often contradictory results. Because of the absence of sufficient power and because of the absence of correction for multiple testing, false positive and negative results (type I and II errors) cannot

be excluded.<sup>3</sup> Findings of negative associations for one selected SNP cannot rule out a potential disease association of the gene in question.

Therefore, researchers today are more aware that it is necessary that each genetic study should assess the haplotype information – that is to say, multiple SNPs – as completely as possible. Genotyping a single variant simply provides no information on a possible disease association of the genetic locus when the outcome is negative. Furthermore, the phenotype classification of periodontitis and control subjects has not been consistent across the various studies. On top of that, many studies have failed to take into account lifestyle factors, potential differences in allele carrier status related to gender, or the presence of comorbidities.

### The GWAS approach

A genome-wide association study (GWAS) is a powerful molecular technique to analyse hundreds of thousands – or even millions – of variations in genomic DNA simultaneously and to determine if any genetic locus is associated with a certain disease phenotype.<sup>4</sup>

GWAS has an open-ended approach, so no *a priori* candidate is investigated. It analyses SNPs covering the entire human genome. This approach will lead

to the discovery of novel candidate genes that have not been known or previously hypothesised – which yields not only new genetic risk factors but also the genetic variants found in GWAS can point to hitherto unknown genes and proteins. This enables the investigation of possible roles in biological pathways, especially in diseases such as periodontitis in which the pathophysiology is not well understood.

The results of an initial GWAS need to be replicated (validated) in an independent case-control cohort with the candidate-gene approach. Until now five GWAS related to periodontitis have been performed.

### Genetic variants

A total of 38 genes have been identified, in which one or several genetic variants have been associated with periodontitis, based on either the candidate-gene approach or GWAS (see Table 1).

Only original genetic studies in which at least 100 cases and at least 100 controls were enrolled were considered in this brief review; however, this low cut-off level may still yield false positive results (type I error).<sup>3</sup>

The table presents a global compilation, summarising the results from studies that have included different ethnicities. The genes which have variant alleles (minor alleles) associated with both AgP and CP, with AgP only, with CP only, or just with periodontitis (PD) are listed in the table in sequence of the number of independent studies available. A given gene with an SNP association with the disease in at least two independent studies provides greater certainty about the validity.

Genetic polymorphisms in four genes (*IL6*, *PTGS2* [*COX2*], *IL10*, and *DEFB1*) are associated with both AgP and CP. The most studied genes are *IL6* and *PTGS2* – five independent studies found an association of minor alleles with both AgP and CP. Genetic variants in seven genes are associated today with AgP only, of which SNPs in *CDKN2B-AS1* (*ANRIL*) seem to be the most robustly validated.

For CP patients, 22 genes have been reported to harbour genetic polymorphisms that have significantly different frequencies compared to controls. The gene *CXCL8* (*IL8*) was found to be positively associated with CP in five independent studies, while each of the other 21 genes is suggested in only one or two independent reports.

Five genes are listed at the end of the table for which gene variants are reported in association with unspecified PD and only in single studies.

Overall, genetic polymorphisms associated with either only AgP, only CP, or both, are mostly located on chromosomes 1 and 6 – five in the first case, seven in the second. These chromosomes may be “hotspots” related to periodontitis.

**Table 1.** The various genes having minor allele frequencies (polymorphisms) significantly associated with periodontitis in independent discovery studies enrolling at least 100 cases and at least 100 controls.2,3,4 The chromosomal location in the genome is indicated and also the association with either AgP or CP or both. The hypothesized/known protein product or (perceived) function of each gene is written in the last column. This table is a global compilation, summarizing the results from studies having included different ethnicities.

| Gene (Alias)*             | Number of independent studies finding an association | Chromosome | AgP, CP or both | Encoded protein or proposed function  |
|---------------------------|--|------------|-----------------|---|
| <i>IL6</i>                | 5  | 7          | Both            | Interleukin-6   |
| <i>PTGS2 (COX2)</i>       | 5  | 1          | Both            | Prostaglandin-Endoperoxide Synthase 2 (Cyclooxygenase-2)  |
| <i>IL10</i>               | 1  | 1          | Both            | Interleukin-10  |
| <i>NPY</i>                | 2  | 7          | Both            | Neuropeptide Y  |
| <i>DEFB1</i>              | 1  | 8          | Both            | Beta-Defensin-1   |
| <i>CDKN2B-AS1 (ANRIL)</i> | 5  | 9          | AgP             | Antisense non-coding RNA in the <i>INK4</i> locus (the regulatory region has an effect on the activity of <i>CAMTA1</i> ) |
| <i>GLT6D1</i>             | 2  | 9          | AgP             | Glycosyltransferase-6 domain 1  |
| <i>FURIN</i>              | 1  | 15         | AgP             | Furin, (Paired Basic Amino Acid Cleaving Enzyme)  |
| <i>PLG (PLASMINOGEN)</i>  | 1  | 6          | AgP             | Plasminogen   |
| <i>CAMTA1</i>             | 1  | 1          | AgP             | Calmodulin Binding Transcription Activator 1  |
| <i>TGFBRAP1</i>           | 1  | 2          | AgP             | Transforming Growth Factor Beta Receptor Associated Protein 1   |
| <i>SLC23A1</i>            | 1  | 5          | AgP             | Solute Carrier Family 23 Member 1 (vitamin C transporter)   |
| <i>AGT</i>                | 1  | 1          | AgP             | Angiotensinogen   |
| <i>NOX4 (NADPH)</i>       | 1  | 11         | AgP             | <i>NADPH</i> Oxidase 4  |
| <i>CXCL8 (IL8)</i>        | 4  | 4          | CP              | C-X-C Motif Chemokine Ligand 8 (Interleukin-8)  |
| <i>VDR</i>                | 2  | 12         | CP ¶            | Vitamin D receptor  |
| <i>MMP1</i>               | 2  | 11         | CP              | Matrix metalloproteinase 1  |
| <i>MMP3</i>               | 2  | 11         | CP              | Matrix metalloproteinase 3  |
| <i>MMP9</i>               | 2  | 20         | CP              | Matrix metalloproteinase 9  |
| <i>IL1B</i>               | 2  | 2          | CP              | Interleukin-1 Beta  |
| <i>AP3B2</i>              | 2  | 15         | CP              | Adaptor protein 3   |
| Composite <i>IL1</i> †    | 1  | 2          | CP              | <i>IL1A</i> and <i>IL1B</i> encoding for Interleukin-1A and Interleukin-1B resp.  |
| <i>NR112 (PXR)</i>        | 1  | 3          | CP              | Nuclear Receptor Subfamily 1 Group I Member 2   |
| <i>CELF2</i>              | 1  | 10         | CP              | CUGBP, Elav-Like Family Member 2 (Bruno-Like Protein 3)   |
| <i>TLR4</i>               | 1  | 9          | CP              | Toll-Like Receptor 4  |
| <i>FBXO38</i>             | 1  | 5          | CP              | F-Box Protein 38  |
| <i>ADGRE1 (EMR1)</i>      | 1  | 19         | CP              | EGF-like Module Receptor 1  |
| <i>NCR2</i>               | 1  | 6          | CP              | Natural Cytotoxicity Triggering Receptor 2  |
| <i>WNT5A</i>              | 1  | 3          | CP              | Wnt Family Member 5A  |
| <i>SERPINE1 (PAI1)</i>    | 1  | 7          | CP              | Serpin Family E Member 1  |
| <i>AGER (RAGE)</i>        | 1  | 6          | CP              | Advanced Glycosylation End-Product Specific Receptor  |
| <i>TGFB1</i>              | 1  | 19         | CP              | Transforming Growth Factor Beta 1   |
| <i>IL4</i>                | 1  | 5          | CP              | Interleukin-4   |
| <i>IL1RN (ILRN)</i>       | 1  | 2          | CP              | Interleukin-1 Receptor Antagonist   |
| <i>MICA</i>               | 1  | 6          | CP              | Major Histocompatibility Complex Class I Chain Related Gene A   |
| <i>MICB</i>               | 1  | 6          | CP              | Major Histocompatibility Complex Class I Chain Related Gene B   |
| <i>NIN</i>                | 1  | 14         | CP              | Ninein Centromosomal Protein  |
| <i>ABHD12B</i>            | 1  | 14         | CP              | Abhydrolase Domain Containing 12B   |
| <i>WHAMM</i>              | 1  | 15         | CP              | WAS Protein Homology Associated with Actin, Golgi Membranes and Microtubules  |
| <i>IL2</i>                | 1  | 4          | CP              | Interleukin-2   |
| <i>DDX39B (BAT1)</i>      | 1  | 6          | PD §            | DEAD-Box Helicase 39B   |
| <i>CYP1A1</i>             | 1  | 15         | PD §            | Cytochrome P450 1A1   |
| <i>GSTM1</i>              | 1  | 1          | PD §            | Glutathione S-transferase M1  |
| <i>LTA</i>                | 1  | 6          | PD §            | Lymphotoxin alpha   |
| <i>NFKBIL1</i>            | 1  | 6          | PD §            | Nuclear-Factor of Kappa Light Polypeptide Gene Enhancer In B-cells Inhibitor-Like 1                                       |

\* Current gene names (previous nomenclature, i.e. alias) based on GeneCards ([www.genecards.org](http://www.genecards.org)).

¶ One study specified CP, another study did not specify cases as either AgP or CP.

§ Not specified whether patients suffered from AgP or CP, just grouped all cases as suffering from periodontitis (PD).

† Ad modum Kornman: Kornman, K.S., Crane, A., Wang, H.Y., di Giovine, F.S., Newman, M.G., Pirk, F.W., Wilson, T.G. Jr, Higginbottom, F.L., Duff, G.W. (1997): The interleukin-1 genotype as a severity factor in adult periodontal disease. *Journal of Clinical Periodontology* 24, 72-77.

## EXPERT VIEW

## Conclusions about genetic factors

Various conclusions can be drawn:

- Genetic factors play a role in the aetiology of periodontitis, and genetics contributes to one of at least five areas of causal factors.
- The contribution from genetics in younger individuals (most often AgP) is higher than in older individuals (most often CP).
- Environmental (a dysbiotic subgingival bacterial biofilm) and lifestyle factors play a more dominant role in the phenotype of the disease in older patients with CP.
- Researchers now hypothesise that epigenetic modifications of genomic DNA may also play a role in older people and as the result of inflammatory and infectious processes.
- Another DNA modification that can occur during life is leukocyte telomere lengthening attrition (LTA). It was found that CP patients have shorter telomere lengths than controls.<sup>5</sup>

In addition, it is interesting to realise that the initial colonisation of the teeth and the subgingival compartment in periodontal health and disease may also be affected by the genetic composition of the host.

Although periodontitis is considered to be a chronic inflammatory disease, the term “infectogenomics” has been proposed for the genetic-environmental interaction.<sup>6</sup> In general, this term describes the influence of the genetic make-up on the acquisition, carriage, and possible outgrowth of microorganisms in a given ecological niche.

The current concept is that periodontitis can develop in a genetically susceptible subject, who has an aberrant host immune response and/or intolerance for (some) gram-negative bacteria. In this way, the hyperactive inflammatory process creates a favourable ecological niche in which proteolytic bacteria can thrive.

This would mean, in the case of periodontitis, that host genetic make-up also plays a role in the composition of the subgingival microbiota, thereby contributing to a dysbiotic biofilm. In this context, a recent study used GWAS to identify genetic signatures for certain “biotypes” of periodontitis patients, including colonisation with certain periodontal pathogens.<sup>7</sup>

### Future challenges

Major challenges lie ahead to unravel further the genetic basis of periodontitis.

In view of the proposed polygenic background, the identification so far of 38 genes is limited.

It should be noted that genetic studies need larger cohorts or case-control biobanks<sup>2,6</sup> and, at present, there is only one biobank of this type in Europe<sup>8</sup> – although European researchers are now joining forces with genetic researchers in the USA.

Another challenge is the phenotypic description and grouping of individuals. All studies to date have used AgP and CP as two distinct phenotypes. However, it may well transpire that this is the same disease, but with a different expression or progression rate, depending on each individual's lifestyle, environmental factors, and comorbidities.

Another task that lies ahead is the development of a validated multicausal model or algorithm that could be applied clinically: a model where it would be possible to include various aetiological factors simultaneously, including a “fingerprint” of genetic variants, which would help patients and clinicians determine both risk of disease development and prognosis of treatment. The recent study by Offenbacher *et al.* (2016) has taken an important step towards this goal.<sup>7</sup>

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**Deon P.M. Chin is a third-year bachelor student in Biomedical Sciences at the University of Amsterdam and is following her internship at the Academic Centre for Dentistry Amsterdam with Prof Loos as her supervisor. She is highly interested in studies into the genetic background of inflammatory diseases.**

# Leading researchers call for global action on prevention, diagnosis, and treatment of periodontal disease

A call for global action to reduce the impact of the burden of periodontal diseases on health and well-being has been issued in a health-policy paper published in the *Journal of Clinical Periodontology (JCP)*, the EFP's scientific journal.

The paper – “Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: A call for global action” – was written by four international experts including *JCP* editor Maurizio Tonetti and EFP past president Søren Jepsen.

It is the final version of the “Perio Focus green paper” that was issued in January 2016 and circulated for stakeholder consultation by the EFP.

Thanks to that consultation, the paper has been endorsed by the EFP, the Asian Pacific Society of Periodontology, the Ibero-Panamerican Society of Periodontics, the International Academy of Periodontology, and 46 national societies of periodontology (including 29 of the 30 EFP-affiliated societies). It is also supported by the American Academy of Periodontology.

The paper notes that the global burden of periodontal diseases remains high, having increased by 57.3% between 1990 and 2010, largely as a consequence of a growing ageing population and increased tooth retention. Severe periodontitis is the sixth most prevalent disease worldwide, with an overall prevalence of 11.2%, affecting about 743 million people.

Overall, periodontitis is responsible for 3.5 million years lived with disability, costs US\$54 billion (€50 billion) per year in lost productivity, and represents a major portion of the annual cost of US\$442 billion (€407 billion) of oral diseases.

It is in this context that the paper's authors propose specific actions in the areas of prevention, detection, and treatment as a way to promote periodontal health and manage the global burden of periodontal diseases.

## Prevention

Prevention is key to oral health, says the paper, and periodontitis can be prevented through the effective management of gingivitis and the promotion of healthy lifestyles.

Two elements are necessary to achieve these objectives: professional instruction in self-performed oral hygiene (such as tooth-brushing and inter-dental cleaning) and an integrated and population-based approach to health education based on the Common Risk Factor Approach, which is strongly advocated by the World Health Organization (WHO).

“A critical element is that prevention should be tailored to individual needs through diagnosis and



The paper and two of its authors, Maurizio Tonetti and Søren Jepsen

risk profiling,” note the authors, who endorse the package of prevention measures advocated by the EFP's 2014 European Workshop on Periodontology on the effective prevention of periodontal and peri-implant diseases.

## Diagnosis

As periodontitis can be “easily diagnosed” via a comprehensive full-mouth periodontal evaluation, the paper says that periodontal probing should be a “key component” of the regular dental visit.

The authors point out that professional approaches to periodontal screening that are both sensitive and inexpensive were introduced more than a quarter of a century ago. Nonetheless, “their routine adoption by all oral healthcare professions has been an elusive objective, and the burden of undiagnosed disease remains high worldwide.”

A three-step approach to periodontal diagnosis is advocated:

- (1) patient self-detection of the symptoms and signs of periodontal disease;
- (2) professional periodontal screening to segment the population into three groups – periodontal health, gingivitis (to plan care to prevent periodontitis), and periodontitis;
- (3) comprehensive periodontal examination and diagnosis to plan appropriate treatment of periodontitis.

## Treatment

The paper notes that there is “overwhelming evidence” that periodontitis can be treated and effectively managed in the majority of cases.

Treatment aims to control gingivitis and periodontitis, to avoid disease progression that leads to tooth loss, to retain functional dentition for life, to preserve self-esteem, and to improve quality of life.

In this context, and noting that the “science supporting periodontal treatment is strong”, the paper lists 14 specific actions that should be taken at the national level in order to improve access to available care by enhancing both public and professional awareness.

## Conclusions

The paper notes that periodontitis can be “prevented, easily diagnosed and successfully treated and controlled following appropriate professional care and long-term secondary prevention.”

However, “various cultural and socio-economic barriers to professional care prevent the public from applying correct preventive approaches, receiving early diagnosis and seeking treatment, resulting in limited progress in improving periodontal health.”

The paper concludes that “a strong and coherent body of evidence allows identification of actionable preventive, diagnostic and therapeutic strategies to effectively promote periodontal health and general well-being, and better manage the socio-economic consequences.”

The paper “Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: A call for global action” was written by Maurizio Tonetti (European Research Group on Periodontology, ERGOPerio, Genova, Italy and Department of Periodontology, Faculty of Dentistry, The University of Hong Kong), Søren Jepsen (Department of Periodontology, University of Bonn, Germany), Lijian Jin (Department of Periodontology, Faculty of Dentistry, The University of Hong Kong), and Joan Otomo-Corgel (Department of Periodontology, University of California Los Angeles, USA).

It is published by the *Journal of Clinical Periodontology* as an open-access document:

<https://doi.org/10.1111/jcpe.12732>



RESEARCH

Journal of Clinical Periodontology

## Latest research

### PERIODONTAL THERAPY

## Tooth loss in generalised aggressive periodontitis: Prognostic factors after 17 years of supportive periodontal treatment

This retrospective longitudinal study assessed the risk of and prognostic factors for tooth loss in patients with generalised aggressive periodontitis (GAgP) after periodontal treatment in a university setting. Fifty-seven patients were examined before and after active periodontal therapy and after various years (ranging from nine to 28) of supportive periodontal therapy. Overall, 98 teeth were lost during active periodontal therapy and 134 during supportive therapy. During supportive therapy, three patients (5%) lost 10 or more teeth, 14 (25%) lost between four and nine teeth, and 40 (70%) lost three or fewer teeth. One third of all patients lost no teeth. The study also showed that nearly 84% of all survived teeth showed stable or improved bone level after

supportive periodontal therapy and that the risk of tooth loss was significantly increased in active smokers, in the upper dental arch, with each millimetre of residual probing pocket depth (PPD), and in teeth with furcation involvement and mobility. The study's conclusion was that, within the provided conservative treatment regimen, GAgP patients lost few teeth.

**Authors:** Christian Graetz, Sonja Sälzer, Anna Plaumann, Peter Schlattmann, Maren Kahl, Claudia Springer, Christof Dörfer, Falk Schwendicke.  
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**Full article:** <http://onlinelibrary.wiley.com/doi/10.1111/jcpe.12725/full>

### IMPLANT THERAPY

## Association between diabetes mellitus/hyperglycaemia and peri-implant diseases: Systematic review and meta-analysis

This systematic review investigated whether hyperglycaemia/diabetes mellitus is associated with peri-implant diseases (peri-implant mucositis and peri-implantitis). The review considered 12 studies for qualitative analysis and seven of these for quantitative analysis. Meta-analyses detected that the risk of peri-implantitis was about 50% higher in diabetes than in non-diabetes. Significantly, among non-smokers, those with hyperglycaemia had 3.39 times higher risk for peri-implantitis compared with those with normoglycaemia. But the association between diabetes and peri-implant mucositis was not statistically significant.

The researchers concluded that, "within its limits that demand great caution when interpreting its findings," the systematic review suggested that diabetes mellitus/hyperglycaemia is associated with a greater risk of peri-implantitis (independently of smoking), but not with peri-implant mucositis.

**Authors:** Alberto Monje, Andres Catena, Wenche S. Borgnakke.  
 Published in *Journal of Clinical Periodontology*, Volume 44, Issue 6 (June 2017).  
**Full article:** <http://onlinelibrary.wiley.com/doi/10.1111/jcpe.12724/full>

## Efficacy of collagen matrix seal and collagen sponge on ridge preservation in combination with bone allograft: A randomised controlled clinical trial

The aim of this randomised controlled clinical trial was to test whether the use of collagen matrix seal (CMS) results in similar hard- and soft-tissue remodelling to that obtained with collagen sponge (CS), four months after alveolar ridge preservation (ARP) in combination with freeze-dried bone allograft (FDBA). Twenty-eight patients were randomly assigned to the two groups. Clinical and radiographic measurements were recorded with the same stent at baseline and four months for standardisation. The flapless technique following a traumatic extraction was used for both types of barrier. The study found that reductions in coronal ridge width and vertical buccal bone resorption were not significantly different, while a slight increase in buccal gingival

thickness at the coronal part was observed in both groups. It concluded that CMS and CS, when combined with FDBA, significantly minimised ridge resorption in all dimensions and maintained buccal soft-tissue thickness in sockets with a buccal plate loss of more than two millimetres, in comparison to previously reported findings recorded after tooth extraction without ARP.

**Authors:** Zuhair S. Natto, Andreas Parashis, Bjorn Steffensen, Rumpa Ganguly, Matthew D. Finkelman, Y. Natalie Jeong.  
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