

## Treatment of stage IV periodontitis

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## **i. TITLE**

***Treatment of Stage IV Periodontitis –The EFP S3 Level Clinical Practice Guideline***

## **ii. SHORT RUNNING TITLE**

Treatment of Stage IV Periodontitis Guideline

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### **Conflict of Interest Statement**

Individual potential conflict of interest forms were completed by all participants and are available on file at the European Federation of Periodontology and extracted in the

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## vi. Abstract and keywords;

### Abstract

**Background:** The recently published Clinical Practice Guideline (CPG) for the treatment of periodontitis in stages I-III provided evidence-based recommendations for the treatment of periodontitis patients, defined according to the 2018 classification. Stage IV periodontitis shares the severity and complexity characteristics of stage III periodontitis, but includes the anatomical and functional sequelae of periodontal attachment loss (tooth flaring and drifting, bite collapse, etc.), that require additional interventions following completion of active periodontal therapy.

**Aim:** To develop a S3 Level CPG for the treatment of stage IV periodontitis, focusing on the implementation of interdisciplinary treatment approaches required to treat/rehabilitate patients following associated sequelae and tooth loss.

**Material and Methods:** This S3 Level CPG was developed by the European Federation of Periodontology (EFP), following methodological guidance from the Association of Scientific Medical Societies in Germany and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) process. A rigorous and transparent process included synthesis of relevant research in 13 specifically commissioned systematic reviews, evaluation of the quality and strength of evidence, the formulation of specific recommendations and a structured consensus process with leading experts and a broad base of stakeholders.

**Findings:** The S3 Level CPG for the treatment of stage IV periodontitis culminated in recommendations for different interventions, including orthodontic tooth movement, tooth splinting, occlusal adjustment, tooth- or implant-supported fixed or removable dental prostheses and supportive periodontal care. Prior to treatment planning, it is critically important to undertake a definitive and comprehensive diagnosis and case evaluation, obtain relevant patient information, and engage in frequent re-evaluations during and after treatment. The periodontal component of therapy should follow the CPG for the treatment of periodontitis in stages I-III.

**Conclusion:** The present S3 Level CPG informs clinical practice, health systems, policymakers and, indirectly, the public on the available and most effective modalities to treat patients

with stage IV periodontitis and to maintain a healthy dentition over lifetime, according to the available evidence at the time of publication.

**Key words:** periodontitis, stage IV, clinical guideline, orthodontic, prosthodontic, dental implant

## **vii. Clinical Relevance**

### ***Scientific rationale for the guideline***

Patients with stage IV periodontitis share the severity and complexity features of stage III periodontitis but, in addition, suffer from the functional sequelae and consequences of tooth loss, frequently associated with advanced periodontitis. This Clinical Practice Guideline (CPG) aimed to provide guidance on the necessary interdisciplinary therapy required to rehabilitate the compromised dentition in such patients. The interventions described in this CPG should be carried out following a rigorous evidence-based and patient-centred decision-making process.

### ***Principal findings***

This guideline was developed using strict and validated methodologies for assuring the best available evidence on the efficacy of the interventions considered, and the most appropriate recommendations based on a structured consensus process, including a panel of experts and representatives from key stakeholder groups.

### ***Practical implications***

The application of this S3 Level Clinical Practice Guideline will allow a consistent, interdisciplinary and evidence-based approach to the management of stage IV periodontitis.

## 1 | INTRODUCTION

### 1.1 | The Health Problem

#### 1.1.1 | Definition

Periodontitis is characterized by progressive destruction of the tooth-supporting apparatus (periodontium), with primary features being clinical attachment loss (CAL), radiographically assessed alveolar bone loss, presence of periodontal pockets and bleeding (Papapanou et al., 2018). Periodontitis is characterised further by defining the stage and grade of the disease: stage captures the severity, extent and distribution of the disease, as well as the anticipated complexity for its management; grade captures additional biological dimensions of the disease including the observed and/or anticipated progression rate, predicted treatment outcomes, and the risk that the disease or its treatment will adversely affect the general health of the patient (Papapanou et al., 2018; Tonetti, Greenwell, & Kornman, 2018).

The management of stages I-III periodontitis has already been described in a previously published Clinical Practice Guideline (CPG) (Sanz, Herrera, et al., 2020). The present CPG focuses on the treatment of stage IV periodontitis. The distinction between periodontitis stage III and stage IV is primarily based on the common sequelae of advanced loss of periodontal tissue support which include: (i) tooth loss, resulting in  $\leq 20$  remaining teeth (10 opposing pairs) (ii) masticatory dysfunction, (iii) tooth mobility grade  $\geq 2$ , (iv) severe alveolar ridge defects, and (v) occlusal collapse (tooth drifting, flaring). These unique features of stage IV periodontitis require treatment of a higher level of complexity, but also necessitate an interdisciplinary approach for rehabilitation of the impaired dentition (Papapanou et al., 2018; Tonetti et al., 2018; Tonetti & Sanz, 2019).

Periodontitis represents a major public health problem due to its high prevalence and associated morbidity. Severe periodontitis, in particular, may lead to disability due to impaired chewing function and aesthetics or edentulism, is a source of social inequality, and significantly impairs quality of life (Tonetti, Jepsen, Jin, & Otomo-Corgel, 2017). In addition,

severe periodontitis has a negative impact on general health and is associated with significant dental care costs (Tonetti et al., 2017).

A major difference between the treatment of periodontitis stages III and IV is the need for a stage IV patient to maintain/re-establish a functional dentition and the necessity for a rigorous supportive care program prior to, throughout, and following the rehabilitation phase of care. It has been shown that patients with stage IV periodontitis, when compared with stage I, have a higher risk of periodontal-related tooth loss over a period of follow-up of 10-30 years (hazard ratio 3.73) (Ravida et al., 2020) as well as a higher risk for pathological tooth migration and other functional consequences (Kwok & Caton, 2007).

### **1.1.2 | Pathophysiology**

Periodontitis is initiated by the accumulation of a dental plaque biofilm at and below the gingival margin which becomes increasingly dysbiotic (Meyle & Chapple, 2015) and which results in dysregulation of the host immune-inflammatory response, which further drives the dysbiosis and results to the destruction of periodontal tissues (Hajishengallis & Chavakis, 2021).

### **1.1.3 | Prevalence**

Periodontitis is the most common chronic inflammatory non-communicable disease of humans. According to data originating from the Global Burden of Disease database, 1.1 billion cases of severe periodontitis were prevalent globally in 2019, and an 8.44% (95% confidence interval -CI- 6.62%-10.59%) increase in the age-standardized prevalence rate of severe periodontitis was observed between 1990 and 2019 (Chen, Zhong, Dong, Wong, & Wen, 2021).

The prevalence of masticatory dysfunction has been found to be similar between women and men and more frequent with older age, and it correlates with systemic health and the number of residual teeth (Helkimo, 1976). In a Swedish population, the prevalence of severe dysfunction was found to be low (Salonen, Hellden, & Carlsson, 1990), but in a population of institutionalized older adults (65 years of more) in Italy, the prevalence of masticatory

dysfunction, mainly caused by untreated edentulism, was 35% and it was associated with all-cause mortality after 9 years (Laudisio et al., 2016).

The prevalence (global age-standardized prevalence) of complete edentulism in 12-year or older individuals, was 4.4% in 1990 and 2.4% in 2010, with incidences of 374 and 205 per 100,000 person-years cases, respectively, with no differences between sexes, and a gradual increase with age, peaking at 65 years (Kassebaum et al., 2014). Geographic differences were evident, with European countries presenting high incidences (Kassebaum et al., 2014). In the USA, data from NHANES 2005-2016 showed 4.5% complete edentulism with 10.3% of subjects lacking a functional dentition (i.e. having only one and up to 19 remaining teeth) (Al-Zahrani, Alhassani, Melis, & Zawawi, 2021). Complete and partial edentulism were more frequent in persons with systemic comorbidities or with a compromised systemic condition (Parker, Thornton-Evans, Wei, & Griffin, 2020). The negative impact of edentulism on quality of life, nutrition and systemic health has been well established (Griffin, Jones, Brunson, Griffin, & Bailey, 2012).

#### **1.1.4 | Consequences of failure to treat**

If no treatment is provided for stage IV periodontitis, or if the treatment is inadequate and/or not comprehensive (e.g., does not result in sufficient rehabilitation or correction of the masticatory dysfunction), the risk of additional loss of tooth-supporting tissues increases and may lead to complete edentulism. Untreated severe periodontitis may result in substantial tooth loss in adults (Ramseier et al., 2017) and ranks 77<sup>th</sup> amongst the one hundred most relevant human conditions resulting in disability (Marcenes et al., 2013).

Severe periodontitis and dental caries account for more years lost to disability than any other human disease (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018).

Furthermore, periodontitis is associated with a range of systemic diseases including diabetes (Sanz et al., 2018), cardiovascular diseases (Sanz, Marco Del Castillo, et al., 2020; Tonetti, Van Dyke, & Working group 1 of the joint EFP/AAP Workshop, 2013) and adverse pregnancy outcomes (Sanz, Kornman, & Working group 3 of joint EFP/AAP Workshop,

2013). It is also independently associated with premature death from all causes or cardiovascular disease (Garcia, Krall, & Vokonas, 1998; Linden et al., 2012; Soder, Jin, Klinge, & Soder, 2007; Soikkonen, Wolf, Salo, & Tilvis, 2000), in particular in multi-morbid populations where the impact of periodontitis is equivalent to having co-morbid diabetes mellitus (Sharma, Dietrich, Ferro, Cockwell, & Chapple, 2016), and also results in increased medical expenditure (Sato, Iwasaki, Yoshihara, & Miyazaki, 2016).

#### **1.1.5 | Financial aspects**

On a global scale, periodontitis of all stages is estimated to cost \$54 billion in direct treatment costs and further \$25 billion in indirect costs (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018). Periodontitis, and especially severe periodontitis (including stages III and IV periodontitis), contributes significantly to the total expenditure allocated to manage dental diseases due to the need to replace lost teeth. In 2015, the total cost of dental diseases was estimated to amount to \$544.41 billion, being \$356.80 billion direct costs (dental expenditures), and \$187.61 billion indirect costs (productivity losses) (Righolt, Jevdjevic, Marcenes, & Listl, 2018).

Although the economic impact of edentulism has not been clearly established, at least two factors may support its importance: on one hand, the need of rehabilitation; on the other hand, and in case of lack of rehabilitation, the negative consequences already listed in quality of life, nutrition, systemic health, etc. In addition, it has also been concluded that individual- and community-level social inequalities have a strong impact of edentulism (Ito et al., 2015).



## **2 | AIM OF THE GUIDELINE**

This guideline aims to highlight the importance of, and need for scientific evidence in, clinical decision making in the treatment of patients with stage IV periodontitis. Its main objective, therefore, is to summarize the evidence-based recommendations for the individual interventions involved in the multidisciplinary management of stage IV periodontitis, based on the best available evidence and/or expert consensus. In so doing, this guideline aims to (i) inform sound therapeutic approaches to the treatment of stage IV periodontitis, and thereby improve the overall quality of periodontal treatment rendered in Europe and worldwide, (ii) reduce tooth loss associated with periodontitis, and ultimately (iii) improve overall systemic health and quality of life.

### **2.1 | Target users of the guideline**

Dental professionals, together with stakeholders related to oral health care, including patients. In addition, this CPG aims to inform medical professions, health systems, policymakers, patients and the public.

### **2.2 | Targeted environments**

Academic/hospital environments, community-based dental clinics and practices.

### **2.3 | Targeted patient population**

People with stage IV periodontitis.

People with stage IV periodontitis, following successful periodontal treatment.

People with stage IV periodontitis, following successful periodontal and multidisciplinary treatment.

### **2.4 | Exceptions from the guideline**

This guideline did not consider in detail the health/economic cost-benefit ratio of the proposed therapies, since (i) the target users and patient populations include people in different countries with diverse, not readily comparable health care systems, and (ii) there is a paucity of sound scientific data available addressing this issue.

This guideline did not consider the treatment of gingivitis (although management of gingivitis is included as an indirect goal in a number of proposed interventions), the treatment of stages I-III periodontitis (already covered in a previously published guideline (Sanz, Herrera, et al., 2020)), necrotising periodontitis (Herrera, Retamal-Valdes, Alonso, & Feres, 2018; Papapanou et al., 2018), periodontitis as manifestation of systemic diseases and mucogingival conditions (Jepsen et al., 2018). However, we emphasize that (i) treatment of gingivitis is a primary prevention strategy for periodontitis (Chapple et al., 2015), and (ii) maintenance of stable periodontal tissues requires the control of gingival inflammation (Chapple et al., 2018).

### 3 | METHODOLOGY

#### 3.1 | General framework

This guideline was developed following methodological guidance published by the Standing Guideline Commission of the Association of Scientific Medical Societies in Germany (AWMF) (<https://www.awmf.org/leitlinien/awmf-regelwerk/awmf-guidance.html>) and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group (<https://www.gradeworkinggroup.org/>).

The guideline was developed under the auspices of the European Federation of Periodontology (EFP) and overseen by the EFP Workshop Committee. This guideline development process was steered by an Organizing Committee and a methodology consultant designated by the EFP. All members of the Organizing Committee participated in the EFP Workshop Committee.

To ensure adequate stakeholder involvement, the EFP established a guideline panel involving dental professionals representing national periodontal societies within the EFP, together with experts in Orthodontics, Prosthodontics, Implant Dentistry, Oral Surgery and Oral Diagnosis (Table 1a). These delegates were nominated and selected by the Organizing Committee and participated in the guideline development process with voting rights in the consensus conference. For the guideline development process, delegates were assigned to four Working Groups that were chaired by selected members of the Organizing Committee and guided by the methodology consultant. This panel was supported by key stakeholders from European scientific societies with a strong professional interest in periodontal care and from European organizations representing key groups within the dental profession (Table 1b), and key experts from non-EFP member regions, such as North America and Australia.

In addition, the EFP engaged an independent guideline methodologist to advise the panel and facilitate the consensus process (Prof. Dr. med. Ina Kopp). The guideline methodologist had no voting rights.

The EFP and the guideline panel attempted to involve patient forums/organizations but were unable to identify any groups focused on periodontal diseases at a pan-European level. In a future update, efforts will be undertaken to include the perspectives of citizens/patients (Brocklehurst et al., 2018), and national societies will be encouraged to involve patient groups within individual countries, as key stakeholders for the *Adaptation, Adoption, De Novo Development* – “ADOLOPMENT” of this GPG (Schunemann et al., 2017).

## **3.2 | Evidence Synthesis**

### **3.2.1 | Systematic search and critical appraisal of guidelines**

To assess and utilize existing guidelines during the development of the present guideline, we performed electronic searches in a range of well-established guideline registers and the websites of large periodontal societies:

- Guideline International Network (GIN)
- Guidelinecentral.com
- The National Institute for Health and Clinical Excellence (NICE)
- Canadian Health Technology Assessment (CADTH)
- European Federation for Periodontology (EFP)
- American Academy of Periodontology (AAP)
- American Dental Association (ADA)

The last search was performed on 1st November 2021. Search terms used were: “periodont\*” “Periodontal”, “Guidelines, “Clinical Practice Guidelines”. In addition, content was screened by hand searches, see Table 2.

Only guidelines published in English and with full texts available were included. The methodological quality of these guideline texts was critically appraised using the AGREE II framework (<https://www.agreetrust.org/agree-ii/>).

We did not identify guidelines/documents directly relevant to the current guideline development process due to: (i) their publication time, which frequently predated the

workshop that defined stage IV periodontitis, (ii) their methodological approach, or (iii) their stated inclusion criteria. We have referenced the EFP S3-level clinical practice guideline (Sanz, Herrera, et al., 2020), where applicable.

### **3.2.2 | Systematic search and critical appraisal of the literature**

For this guideline, a total of 13 systematic reviews (SRs) were conducted to support the guideline development process (Carra et al., 2021; Dommisch et al., 2021; Donos, Andre Mezzomo, Mardas, Goldoni, & Calciolari, 2021; Gennai, Izzetti, Pioli, Music, & Graziani, 2021; Gotfredsen, Rimborg, & Stavropoulos, 2021; Kloukos et al., 2021; Leow et al., 2021; Martín et al., 2021; Montero et al., 2021; Orlandi et al., 2021; Papageorgiou et al., 2021; Ramanauskaite, Becker, Wolfart, Lukman, & Schwarz, 2021; Tomasi, Albouy, Schaller, Navarro, & Derks, 2021). The corresponding manuscripts are published within this special issue of the Journal of Clinical Periodontology. The systematic reviews were updated in July-September 2021, and are presented as an Addendum to the present CPG. The Addendum is available as Supporting Information, accessible on line ([CPGstage4-Addendum](#)).

All SRs were conducted following the “Preferred Reporting Items for Systematic Reviews and Meta-Analyses” (PRISMA) framework (Moher, Liberati, Tetzlaff, & Altman, 2009), and were prospectively registered in PROSPERO.

### **3.2.3 | Focused questions**

In all 13 systematic reviews, focused questions in PICOS format (Guyatt et al., 2011) were proposed by the authors in January 2019 to a panel comprising the working group chairs and the methodological consultant in order to review and approve them (Table 3). The panel took great care to avoid overlaps between the SRs or significant thematic omissions, in order to ensure that they encompass the main interventions currently undertaken in the management of stage IV periodontitis.

### **3.2.4 | Relevance of outcomes**

One important outcome of interest in a clinical guideline in Dentistry is tooth loss. However, a narrative review article (Loos & Needleman, 2020), commissioned during the development of the CPG for the treatment of stage I-III periodontitis (Sanz, Herrera, et al., 2020) reported

that the reduction in periodontal probing pocket depth (PPD) was an important predictor of tooth loss, in the context of periodontal therapy. Therefore, PPD reduction was also used as a primary outcome in systematic reviews not addressing periodontal regeneration, and in instances where tooth loss data were not available. When reviewing regenerative interventions, gains in clinical attachment were used as the primary outcome measure. Secondary periodontal outcomes included the proportion of residual/open pockets as critical endpoint of therapy, which have been shown to be associated with disease recurrence (Loos & Needleman, 2020).

For the purposes of the present guideline, in addition to tooth survival, tooth-supported prosthesis survival as well as implant and implant-supported prosthesis survival were also considered. Additional outcomes related to complexity factors were also addressed in the SRs (e.g. vertical dimension or evaluation of masticatory dysfunction). Finally, patient-related outcome measures (PROMs), quality of life indicators and economic factors were studied whenever possible.

### **3.2.5 | Search strategy**

All SRs utilized a comprehensive search strategy of at least two different databases, supplemented by a hand search of periodontology-focused journals and the reference lists of included studies. In all SRs, the electronic and manual search, as well as the data extraction, was undertaken in parallel by, at least, two different investigators.

### **3.2.6 | Quality assessment of included studies**

In all SRs, the risk of bias of controlled clinical trials was assessed using the Cochrane Risk-of-bias tool (<https://methods.cochrane.org/bias/resources/rob-2-revised-cochrane-risk-bias-tool-randomized-trials>). For observational studies, the Newcastle-Ottawa-Scale was used ([http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp)).

### **3.2.7 | Data synthesis**

Where applicable, the available evidence was summarized by means of a meta-analysis.

## **3.3 | From Evidence to Recommendation: Structured Consensus Process**

The structured consensus development conference was held during the XVII European Workshop in Periodontology in La Granja de San Ildefonso Segovia, Spain, on November 7th – 9th, 2021. Using the 13 SRs as background information, evidence-based recommendations were formally debated by the guideline panel using the format of a structured consensus development conference. This consisted of small group discussions and open plenary discussions, where the proposed recommendations were presented, voted upon and adopted by consensus (Murphy et al., 1998). Delegates declaring potential conflicts of interest abstained from voting and abstentions were recorded. Prior to the in-person meeting, up to four online meetings were organized (one at the plenary level, and three at the working group level) in July, September and October 2021, in order to advance the process of guideline development to a mature stage prior to the face-to-face consensus meeting.

In the small group phase, delegates convened in four working groups (WGs) directed by two chairpersons belonging to the EFP Workshop Committee, addressing the following subtopics:

- WG 1. Treatment of pathological tooth migration in stage IV periodontitis patients (chairs Søren Jepsen and Mariano Sanz).
- WG 2. Treatment of tooth loss/masticatory dysfunction/bite collapse in stage IV periodontitis patients - partial edentulism amenable for partial rehabilitation (chairs Moritz Kepschull and Anton Sculean).
- WG 3. Treatment of tooth loss/masticatory dysfunction/bite collapse in stage IV periodontitis patients with a terminal dentition only amenable for full-arch rehabilitation (chairs Tord Berglundh, Panos Papapanou and Maurizio Tonetti).
- WG 4. Long-term outcomes and impact of treatment in stage IV periodontitis patients (chairs Iain Chapple and David Herrera).

With the support of the methodology expert, recommendations and draft background texts were generated and subsequently presented, debated and subjected to a vote in the plenary sessions with all delegates present. During these plenary sessions, the guideline development process and discussions and votes were overseen and facilitated by the

independent guideline methodologist (I.K.). The plenary votes were recorded using an electronic voting system, checked for accuracy and then introduced into the guideline text.

The consensus process was conducted as follows:

### **3.3.1 | Plenary 1 (on line session, July 2021)**

Introduction to guideline methodology (presentation, discussion) by the independent guideline methodologist (I.K.) and the chair of the workshop (D.H).

### **3.3.2 | Working group Phase 1 (three on line sessions, from July to October 2021)**

- Peer evaluation of declarations of interest and management of conflicts of interest.
- Presentation of the evidence (SR results) by group chairs and reviewers.
- Invitation of all members of the working group to reflect critically on the quality of available evidence by group chairs, considering the GRADE criteria.
- Structured group discussions:
  - o development of draft recommendations and their grading, considering the GRADE-criteria.
  - o development of draft background texts, considering the GRADE-criteria.
  - o invitation to comment on draft recommendations and background text to suggest reasonable amendments by group chairs.
  - o collection and merging of amendments by group chairs.

### **3.3.3 | Plenary 2 (in-person meeting, November 2021)**

- Presentation of working group results (draft recommendations and background text) by Working Group chairs.
- Invitation to formulate questions, statements and reasonable amendments of the plenary by the independent guideline methodologist /facilitator.
- Answering of questions by working group chairs.
- Collection and merging of amendments by an independent moderator.
- Preliminary vote on all suggestions provided by the working groups and all reasonable amendments.
- Assessment of the strength of consensus.



- Recording of abstentions made due to potential conflicts of interest.
- Opening debate, where no consensus was reached or reasonable need for discussion was identified.
- Formulation of tasks to be solved within the working groups.

#### **3.3.4 | Working Group Phase 2 (in-person meeting, November 2021)**

- Discussion of tasks and potential amendments raised by the plenary.
- Formulation of reasonable and justifiable amendments, considering the GRADE framework.
- Initial voting within the working group on recommendations and guideline text for plenary.

#### **3.3.5 | Plenary 3 (in-person meeting, November 2021)**

- Presentation of working group results by working group chairpersons.
- Invitation to formulate questions, statements and reasonable amendments of the plenary by the independent moderator.
- Collection and merging of amendments by independent moderator.
- Preliminary vote.
- Assessment of the strength of consensus.
- Opening debate, where no consensus was reached or reasonable need for discussion was identified.
- Formulation of reasonable alternatives.
- Final vote of each recommendation, recording the consensus and abstentions due to potential conflicts of interest.

#### **3.3.6 | Plenary 3 (online meeting, January 2022)**

- Presentation of pending recommendations and suggestions received.
- Preliminary vote.
- Assessment of the strength of consensus.
- Opening debate, where no consensus was reached or reasonable need for discussion was identified.
- Formulation of reasonable alternatives.

- Final vote of each recommendation, recording abstentions due to potential conflicts of interest.

### **3.4 | Definitions: Rating the Quality of Evidence, Grading the Strength of Recommendations and Determining the Strength of Consensus**

For all recommendations and statements, this guideline makes transparent:

- the underlying quality of evidence, reflecting the degree of certainty / uncertainty of the evidence and robustness of study results
- the grade of the recommendation, reflecting the criteria considered to make the judgement; the strength of consensus, indicating the degree of agreement within the guideline panel; the number of abstentions due to potential conflicts of interest.

#### **3.4.1 | Quality of Evidence**

The quality of evidence was assessed using a recommended rating scheme (Balshem et al., 2011; Schunemann, Zhang, Oxman, & Expert Evidence in Guidelines, 2019).

#### **3.4.2 | Strength of Recommendations**

The grading of the recommendations used the grading scheme (Table 4) by the (German Association of the Scientific Medical Societies (AWMF) & Standing Guidelines Commission, 2012), taking into account not only the quality of evidence, but also considered judgement guided by the following criteria:

- relevance of outcomes and quality of evidence for each relevant outcome
- consistency of study results
- direct applicability of the evidence to the target population/PICOS specifics
- precision of effect estimates using confidence intervals
- magnitude of the effects
- balance of benefit and harm
- ethical, legal, economic considerations
- patient preferences

The grading of the quality of evidence and the strength of a recommendation may therefore differ, but where they do, the justification and context is clearly documented in the background narrative that follows each recommendation table.

### **3.4.3 | Strength of Consensus**

The consensus determination process followed the recommendations by the (German Association of the Scientific Medical Societies (AWMF) & Standing Guidelines Commission, 2012). Where consensus could not be reached, different points of view were documented in the guideline text (see Table 5).

## **3.5 | Editorial Independence**

### **3.5.1 | Funding of the guideline**

The development of this guideline and its subsequent publication was financed entirely by internal funds of the European Federation of Periodontology (EFP), without any support from industry or other organisations.

### **3.5.2 | Declaration of Interests and Management of Potential Conflicts**

All members of the guideline panel declared secondary interests using the standardized form provided by the International Committee of Medical Journal Editors (ICMJE) (International Committee of Medical Editors).

Management of conflicts of interests (ColS) was discussed in the working groups and the plenary sessions, following the principles provided by the Guidelines International Network (Schunemann et al., 2015). According to these principles, panel members with relevant, potential ColS abstained from voting on guideline statements and recommendations within the consensus process. Those abstentions were recorded in each recommendation table.

## **3.6 | Peer review**

All 13 systematic reviews underwent a multi-step peer review process. First, the draft documents were evaluated by members of the EFP Workshop Committee and the methodological consultants using a custom-made appraisal tool to assess: (i) the

methodological quality of the SRs using the AMSTAR 2 checklist (Shea et al., 2017), and (ii) whether all PICOS questions were addressed as planned. Detailed feedback was then provided for the SR authors. Subsequently, all 13 systematic reviews underwent the regular editorial peer review process defined by the *Journal of Clinical Periodontology*. In addition, the reports of the updates of the SRs, presented in the Addendum, were also peer-reviewed.

The guideline text was drafted by the chairs of the working groups, in close cooperation with the methodological consultant, and circulated among the members of the guideline group prior to the Workshop. The methodological quality was formally assessed by an external consultant using the AGREE framework. The guideline was subsequently peer reviewed for its publication in the *Journal of Clinical Periodontology* following the standard evaluation process of the journal.

### **3.7 | Implementation and dissemination plan**

For this guideline, a multi-stage dissemination and implementation strategy will be established and implemented by the EFP, supported by a communication campaign.

This will include:

- Publication of the guideline and the underlying systematic reviews as an Open Access special issue of the *Journal of Clinical Periodontology*.
- Local uptake from national societies, either by Commentary, Adoption, or Adaptation (Schunemann et al., 2017).
- Generation of educational material for dental professionals and patients, and dissemination via the EFP member societies.
- Dissemination via educational programs at dental conferences.
- Dissemination via the EFP through European stakeholders via National Society members of the EFP.
- Long-term evaluation of the successful implementation of the guideline by a survey of EFP members.

The timeline of the guideline development process is detailed in Table 6.

### **3.8 | Validity and update process**

The guideline is valid until 2027. However, the EFP, represented by the members of the Organizing Committee, will continuously assess current developments in the field. Where there are major changes of circumstances, e.g., new relevant evidence, this will trigger an update of the guideline to potentially amend the recommendations. It is planned to update the current guideline regularly on demand and consistent with the format of a living guideline.

## **4 | PERIODONTAL DIAGNOSIS AND TREATMENT SEQUENCE FOR THE MANAGEMENT OF STAGE IV PERIODONTITIS PATIENTS**

### **4.1 | Periodontal diagnosis**

Defining a case of periodontitis and establishing a diagnosis should be performed using the 2018 classification system, developed following the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions (Caton et al., 2018; Chapple et al., 2018; Jepsen et al., 2018; Papapanou et al., 2018; Tonetti et al., 2018).

According to this classification, stage IV periodontitis is identified from the broader population of individuals with stage III periodontitis, defined by periodontal inflammation, and attachment loss reaching the middle third of the root and beyond, based on the presence of one or more of the following criteria:

- Secondary occlusal trauma/tooth hypermobility attributable to a reduced periodontal attachment that is attributed to periodontitis.
- Tooth migration, drifting, opening of diastema is associated with severe attachment loss at the affected teeth.
- Loss of more than four teeth due to periodontitis.
- Loss of posterior support and/or flaring of anterior teeth due to periodontitis.
- Loss of masticatory function (masticatory dysfunction) secondary to a combination of the above.

The above signs and symptoms of functional impairment (masticatory dysfunction) may also be present as sequelae of multiple tooth loss due to caries or severe malocclusion in people without significant periodontal breakdown or even in people with periodontal breakdown compatible with stages I-II periodontitis, who do not meet the criteria for stage IV. Hence, differential diagnosis is important.

Stage IV periodontitis not only jeopardizes the survival of individual teeth, but that of the entire dentition. In these patients, control of periodontitis (through standard periodontal therapy, i.e., steps I-III plus supportive periodontal care) is not enough to stabilize the

mouth, resolve masticatory dysfunction and improve quality of life. An interdisciplinary treatment plan, that may include the management of secondary occlusal trauma, orthodontic tooth movement and/or restorative dental care following successful periodontal therapy, must therefore be implemented to adequately treat these patients.

#### **4.1.1 | Specific diagnostic pathways in patients with stage IV periodontitis**

The clinical assessment of a stage IV periodontitis case comprises five critical dimensions:

i) **Evaluation of the amount of periodontal breakdown, patient function and aesthetics**

A full periodontal examination/charting, combined with appropriate imaging, is required to assess the severity of the periodontal attachment loss and, hence, the complexity of treatment required. In stage IV periodontitis, such examinations must be complemented with an in-depth assessment of the functional and aesthetic status of the individual teeth and the overall dentition, including assessment of tooth hypermobility, assessment of tooth vitality, presence of secondary occlusal trauma, presence of stable posterior vertical stops, fremitus in centric occlusion and excursive movements, subjective and objective assessments of chewing function, aesthetics, and phonetics.

ii) **Number of teeth that have been lost due to periodontitis**

Attributing missing teeth to periodontitis is challenging as it requires a complex assessment based on history of tooth loss/extraction and the symptoms associated with it (Ravida et al., 2021; Sanz, Papapanou, Tonetti, Greenwell, & Kornman, 2020; Uy et al., 2021). Recall bias and availability of previous records may influence the findings. Nevertheless, the use of a clinical history for the determination of the probable cause of tooth loss adds useful information that can be applied for individual case diagnosis (Ravida et al., 2021).

iii) **Prognosis of individual teeth**

Establishment of tooth prognosis in stage IV periodontitis patients, and especially the differentiation of compromised/questionable teeth from those of hopeless

prognosis is complex and requires a multidisciplinary approach to identify the ability of treatment(s) that may change the assigned prognosis, which is usually linked to the experience and technical ability of the individual operator(s). Individual tooth prognosis is frequently complicated by the need to assess the possibility of a periodontally compromised tooth that is to be used as an abutment for a fixed or a removable restoration. Studies focusing on periodontal prognosis have shown that it is difficult to accurately predict tooth survival, something that even specialists tend to underestimate (McGuire & Nunn, 1996). Key for long-term prognosis is the ability to achieve the endpoints of periodontal therapy that were identified in the guideline for the treatment of periodontitis in stages I-III (Loos & Needleman, 2020; Sanz, Herrera, et al., 2020), and the implementation of an effective supportive periodontal care program.

iv) **Restorative factors**

The extent of the edentulous spaces, as well as the number, distribution and restorability of teeth that can be retained must be assessed, whilst considering all restorative scenarios, either focusing on teeth alone and/or with the addition of dental implants. These scenarios must consider the technical complexities of the planned prosthesis, as well as the interventions required to place implants, depending on the availability of adequate ridge dimensions.

v) **Prognosis of the overall case**

The overall case prognosis must be established whilst considering the individual susceptibility of the patient, based on a thorough analysis of the patient's modifiable and non-modifiable risk factors, using the primary grade criteria as well as the grade modifiers defined earlier (Papapanou et al., 2018; Tonetti et al., 2018). The prognosis should also estimate the probability of disease recurrence/progression, which is a differentiator in the management of stage IV periodontitis patients from other complex restorative cases (Baumer et al., 2011; Lang, Suvan, & Tonetti, 2015; Lang & Tonetti, 1996).



The case analysis required to make a sound prognostic assessment and an appropriate treatment plan is complex and requires a detailed assessment of what is technically and biologically feasible, cost-effective and in line with the patient's preferences and expectations.

#### **4.1.2 | Differential diagnosis**

For the practical implementation of the case definition and treatment planning, an appropriate differential diagnoses should be established based on the identification of cases with:

- Opening of diastemata or tooth migration secondary to orthodontic relapse.
- Primary occlusal trauma in people with periodontitis.
- Masticatory dysfunction in people who have experienced multiple tooth loss that cannot be attributed to periodontitis and in the absence of periodontitis.
- Masticatory dysfunction in people who have experienced multiple tooth loss that cannot be attributed to periodontitis, but in the presence of stage I-II periodontitis or localized stage III periodontitis
- Generalized stage III periodontitis without tooth loss, or without the other criteria that define stage IV periodontitis. This differential diagnosis may be difficult in some borderline cases. A recent cross-sectional study, with limited external applicability (Uy et al., 2021), has shown that stage IV periodontitis cases, when compared with other periodontitis cases, were more likely to present more severe periodontal breakdown, tooth hypermobility and loss of posterior functional tooth units, as well as self-reporting changes in dietary habits due their oral condition, impaired chewing ability and lower quality of life.

#### **4.1.3 | Phenotypic variation and identification of clinical case types**

Stage IV periodontitis cases may present with great phenotypic variation based on the individual patterns of their periodontal breakdown, number of missing teeth, intermaxillary relationships and residual alveolar ridge, which will result in different degrees of functional and aesthetic compromise, as well as different treatment needs.

To provide a simplified workable guideline, four major stage IV periodontitis phenotypes were recognised by the organizing committee, leading to specific clinical case types:

- Case type 1: the patient with tooth hypermobility and secondary occlusal trauma that can be corrected without tooth replacement.
- Case type 2: the patient with pathological tooth migration, characterised by tooth elongation, drifting and flaring, which is amenable to orthodontic correction.
- Case type 3: partially edentulous patients that can be prosthetically restored without full-arch rehabilitation.
- Case type 4: partially edentulous patients that need to be restored with full-arch rehabilitation, either tooth- or implant-supported/retained.

These phenotypes and associated clinical case types may overlap on occasion, as one arch may require treatment according to a specific scenario while the other might require a different approach. Furthermore, after orthodontic treatment, it is frequently necessary to retain the teeth in the new position with a fixed type of retainer/splint. Systematic reviews covering the specific scenarios have been commissioned and have been used as the basis for development of this clinical guideline.

Several treatment tools are available for the rehabilitation of the different case types, besides the treatment of periodontitis according to the Guideline for the treatment of periodontitis in stages I-III (Sanz, Herrera, et al., 2020):

- Orthodontic therapy.
- Temporary control of secondary occlusal trauma (e.g. extra-coronal splinting and/or relief of fremitus by limited selective occlusal adjustment).
- Prosthetic splinting with a fixed dental prosthesis.
- Tooth-supported/retained removable or fixed partial dental prostheses.
- Implant-supported/retained removable or fixed partial dental prostheses.
- Tooth supported/retained cross-arch dental prostheses, conventional full dental prostheses, implant-retained or -supported full dental prostheses.

The following **key messages** should be highlighted:

- Most cases of stage IV periodontitis can be successfully treated, maintaining teeth and the natural dentition in a state of adequate health and function.
- Before treatment planning of people with stage IV periodontitis, it is recommended undertaking a full diagnosis and case-study, including a tooth-by-tooth prognosis to identify the number, distribution, residual support, periodontal maintainability, and restorability of the remaining natural dentition.

#### **4.2 | Sequence for the treatment of stage IV periodontitis**

The treatment plan for the management of stage IV periodontitis should include a successful outcome after completing the interventions in steps 1, 2 and 3, according to the EFP S3 Level Clinical Practice Guideline for Treatment of Stage I-III Periodontitis (Sanz, Herrera, et al., 2020). The sequence of the different steps, however, requires the introduction of specific additional treatment measures to meet the specific demands of stage IV periodontitis. In these cases, rehabilitation of function, restoration of masticatory comfort and treatment of secondary occlusal trauma and, sometimes, restoration of the vertical dimension of the occlusion, are also necessary and need to be planned from the beginning, and even implemented simultaneously with steps 1-3.

As is the case for the treatment of periodontitis in stages I-III, an essential pre-requisite to therapy is to inform the patient of the diagnosis, including aetiology of the condition, risk factors, treatment alternatives and expected risks and benefits, including the option of no treatment. This discussion should be followed by agreement on a personalized care plan. The plan might need to be modified during the course of treatment, depending upon initial treatment outcomes, patient preferences, clinical findings, and changes to the patient's overall state of health. It must be recognized that in stage IV periodontitis, a "no treatment" option must be discouraged, given the expected high risk of loss of the dentition.

Key to the care of these patients is:

- The need to combine periodontal therapy, that is modelled in line with the recent guidelines for the treatment of stage I-III periodontitis (Sanz, Herrera, et al., 2020), with rehabilitation.

- Identification of the appropriate timing/sequence of implementation of the adjunctive orthodontic/restorative treatment and the periodontal treatment (Figure 1).

For details of recommended approaches to periodontal therapy, readers are referred to the Guideline for periodontal therapy for stage I-III periodontitis (Sanz, Herrera, et al., 2020), since that guideline also applies to the periodontal treatment of stage IV periodontitis patients. Of particular importance are the frequent re-evaluations to assess adherence to oral hygiene instructions for supragingival biofilm control and adherence to risk factor control interventions, and the two periodontal re-evaluation assessments following step 2, and later after step 3 (“final re-evaluation”), since achieving the desired treatment outcomes is particularly important in stage IV cases to be suitable to proceed with the planned restorative or orthodontic treatment, as well as to justify the significant resources required to proceed with the case. In stage IV periodontitis patients, re-evaluation following step 2 and 3 treatment requires additional planning over and above purely periodontal maintenance. Restorative factors need to be adequately assessed. For example, the ability of a tooth to act as an abutment for a restoration needs to be assessed in terms of periodontal maintainability, but also residual periodontal support and restorative parameters such as the presence of adequate tooth structure. Similarly, dental implants that have been placed to assist in the restoration should present with healthy, maintainable soft- and hard-tissue interfaces.

When evaluating periodontal outcomes at the end of active periodontal treatment (control of periodontal inflammation, achievement of shallow maintainable pockets, management of furcation lesions), it is important to consider whether a specific tooth will be incorporated as an abutment for a fixed or removable prosthesis. Specific criteria must be considered to assess the ability of the tooth to function as a restorative abutment. Whilst it has been shown that teeth with a reduced but healthy periodontium can function well as prosthetic abutments, a minimal threshold of residual periodontal support (10-20%) may be controversial and dependent upon the design of the restoration (e.g., fixed versus removable), the number and distribution of the abutments and the stability of the definitive prosthesis (Nyman & Lang, 1994).

#### 4.2.1 | Specific treatment pathways according to the different stage IV periodontitis case types

Common to all clinical case types is the need to perform a careful diagnosis and a case study that includes both periodontal and rehabilitation phases (orthodontics and/or restorative dentistry, as appropriate). Furthermore, adequate self-performed oral hygiene, and risk factor control must be realised, alongside satisfactory initial treatment outcomes prior to progressing the case to subsequent periodontal/oral rehabilitation.

- **Case type 1:** the patient with tooth hypermobility and secondary occlusal trauma that can be corrected without tooth replacement.

Temporary tooth splinting and initial occlusal adjustment (mostly relief of fremitus in combination with splinting) can be implemented during step 1 of therapy to manage secondary occlusal trauma and the impact of tooth hypermobility on patient comfort. The need for and the implementation of longer-term splinting needs to be re-assessed following completion of steps 2 and 3 of periodontal therapy.

- **Case type 2:** the patient with pathological tooth migration, characterised by tooth elongation, drifting and flaring, which is amenable to orthodontic correction. The orthodontic treatment can be planned during step 2 of care (subgingival instrumentation with or without adjunctives) and, in some cases, step 3 (subgingival re-instrumentation and periodontal surgery) of treatment, but should not be implemented before achieving the periodontal treatment objectives of shallow maintainable pockets and control of periodontal inflammation. Special considerations apply to the regenerative treatment of intrabony defects (Section 7, Figure 2).

- **Case type 3:** partially edentulous patients who can be prosthetically restored without full-arch rehabilitation.

The timing of intermediate restorations, if required, should be carefully evaluated based on the individuality of the case and keeping in mind patient wishes and aesthetic considerations. Ideally, interim tooth-retained restorations or dental implants should not be placed before completion of step 2 of treatment and, if possible, deferred until

the periodontal treatment objectives have been achieved (after re-evaluation following steps 2 and 3 of periodontal treatment). Definitive restorative treatment or placement of dental implants must be performed after successful completion of periodontal therapy and any additional conservative treatment of the abutment teeth.

- **Case type 4:** partially edentulous patients that need to be restored by means of full-arch rehabilitation, either tooth- or implant-retained, and either fixed or removable.

The timing of treatment differs for cases with tooth-supported full-arch restorations and cases with implant-supported full-arch restorations.

In tooth-supported cases, an intermediate restoration is frequently placed following successful completion of step 1 of periodontal treatment. Step 2 of periodontal treatment, including scaling and root surface instrumentation of the abutment teeth, is performed with the intermediate restoration in place. Insertion of a definitive restoration (or long-term intermediate restoration) follows successful completion of periodontal therapy and achievement of shallow maintainable pockets and control of periodontal inflammation.

For implant-supported cases requiring extraction of the terminal dentition, in one or both arches, teeth are extracted, and implants placed after successful completion of step 1 of periodontal treatment. The sequence of treatment and the insertion of intermediate fixed or removable prostheses aims to reconcile the biology of wound healing with the need to manage patient expectations and ensure an adequate level of comfort during the transition.

#### **4.2.2 | Additional therapeutical interventions in stage IV periodontitis**

The present Guideline has specifically focused on the additional interventions for stage IV periodontitis patients, including:

- Temporary control of secondary occlusal trauma (e.g. extra-coronal splinting and/or relief of fremitus by limited selective occlusal adjustment) (section 6).
- Orthodontic therapy (section 7).
- Rehabilitation of one or multiple (small or large) tooth-delimited edentulous spaces (section 9).

- Rehabilitation of unilateral or bilateral posterior free-end edentulism (section 9).
- Tooth-supported full-arch fixed dental prostheses (section 10).
- Tooth-supported full-arch removable dental prosthesis (section 10).
- Implant-supported full-arch fixed dental prostheses (section 10).
- Implant-supported removable dental prosthesis (section 10).

Some of these interventions should be **performed simultaneously or within steps 1-3** of periodontal therapy, including relief of pain, symptoms of tooth hypermobility, functional impairment, and conservative treatment of the dentition (including abutment teeth).

Restorative treatment implemented during steps 1-3 of periodontal therapy usually consists of intermediate restorations that will only be replaced with definitive ones after final evaluation of the case and achievement of the periodontal and restorative objectives.

Conversely, certain other interventions will only be **performed in a last step (*Step R, for rehabilitation*)**, following successful completion of steps 1-3 periodontal therapy, once the patient has started supportive periodontal care, and after achievement of the periodontal and restorative treatment objectives. *Step R* treatment includes:

- Long-term periodontal splinting.
- Orthodontic tooth movement and retention.
- Definitive restorations designed to satisfy the functional and aesthetic demands of the patient and enable optimal self-performed oral hygiene and professional tooth cleaning during supportive periodontal care.

#### **4.2.3 | Supportive periodontal care in stage IV periodontitis patients**

As for the treatment of stage I-III periodontitis (Sanz, Herrera, et al., 2020), supportive periodontal care (Trombelli, Franceschetti, & Farina, 2015) is a crucial step to achieve periodontal stability and long-term tooth/implant retention. This Guideline provides specific recommendations for supportive periodontal care in stage IV periodontitis patients (section 11).

#### **4.2.4 | Impact of therapy in stage IV periodontitis patients on systemic health and quality of life**

It is well established that, in addition to positive effects on periodontal outcomes, periodontal therapy may also impact favourably upon systemic health (e.g., reduce systemic inflammation and lower the levels of markers of cardiometabolic risk) and on quality of life. Since the treatment of stage IV periodontitis includes both periodontal therapy and rehabilitation, the impact of both interventions were considered within the present Guideline and recommendations are presented for both the impact of periodontal therapy (section 12.1) and the impact of rehabilitation (dental prostheses) in fully or partially edentulous patients (section 12.2).

We highlight the following **key messages**:

- To effectively manage stage IV periodontitis, it is recommended that patients are informed in detail about their condition, the various treatment options and associated risks, including the need for periodontal therapy, the design of the rehabilitation, and the sequence of interventions. In addition, patients should be aware that treatment planning may be modified depending upon several factors, including treatment outcomes at re-evaluations, and adherence/compliance with interventions, such as supragingival biofilm control, or risk factor control.
- The starting point for treatment of stage IV periodontitis initially attempts to preserve all periodontally compromised teeth that are deemed rational to treat. Early extraction of teeth with questionable (as opposed to hopeless) prognosis is strongly discouraged and is not supported by current evidence.
- Whenever tooth retention is possible, it is recommended that periodontal treatment of stage IV periodontitis patients should follow the Guideline for the treatment of periodontitis in stages I-III. In these patients, the ability to successfully complete full periodontal therapy is a pre-requisite. In addition, management of these cases may also include orthodontics, tooth splinting, tooth-supported fixed and removable dental prostheses, and/or implant-supported fixed and removable dental prostheses.
- For stage IV periodontitis patients, it is recommended to frequently assess motivation and adherence to self-performed supragingival plaque control and risk factor control



throughout the course of treatment and during supportive periodontal care, since this will greatly influence both the choice and the outcomes of therapy.

- In stage IV periodontitis patients, it is recommended that restorations should be designed to achieve function and aesthetics while enabling effective self-performed oral hygiene and professional tooth cleaning.

The first part of this CPG document (sections 1-4) was prepared by the steering group with the help of the methodology consultant, it was examined by the experts participating in the consensus and section 4 was voted upon in a plenary session to form the basis for the specific recommendations.

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| <p><b><i>Strength of consensus</i></b> Unanimous Consensus (0% of the group abstained due to potential Col)</p> |
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## 5 | CLINICAL RECOMMENDATIONS – OVERALL STRATEGY FOR THE MANAGEMENT OF STAGE IV PERIODONTITIS PATIENTS

The pathognomonic feature of stage IV periodontitis, as explained in section 4, is the functional and aesthetic compromise secondary to the periodontal tissue breakdown and the tooth loss caused by the disease process. This process severely impacts the quality of life and puts the dentition at risk of being lost if appropriate treatment is not rendered. As discussed, the disease spectrum covers a wide range of phenotypic variations characterized by a wide spectrum from subtle changes, that may be overlooked, to severe loss of function that raises the question of whether the dentition can be saved, and rehabilitation of function can translate in restoration of quality of life. The competences required for appropriate diagnosis and management of these cases are frequently complex and interdisciplinary while the evidence base supporting the different choices is frequently limited. In such situation of complexity and uncertainty the experts and stakeholders participating in the workshop agreed on a series of expert-based recommendations that provide critical guidance in the management of these cases, in order to understand the general strategical principles for therapeutic management in patients with a compromised dentition due to stage IV periodontitis.

### R5.1 | Can stage IV periodontitis can be successfully managed?

|  |
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| <b>Additional question raised by the WG</b>  |
| <b>R5.1 - Expert consensus-based statement</b>   |
| <i>Stage IV periodontitis can be successfully managed with the combination of periodontal therapy, appropriate rehabilitation of function and improvement of esthetics/quality of life, and supportive periodontal care.</i> |
| <b>Supporting literature</b> Expert opinion  |
| <b>Quality of evidence</b> Not applicable  |
| <b>Grade of recommendation</b> Statement   |
| <b>Strength of consensus</b> Unanimous Consensus (0% of the group abstained due to potential Col)  |

#### Background

Experts wished to emphasize that stage IV periodontitis can be managed beyond the scope of palliative care and that management requires appropriate periodontal therapy delivered

according to the S3 Guideline for management of stage I-III periodontitis (Sanz, Herrera, et al., 2020) in combination with rehabilitation of lost function. Once active treatment is completed, supportive periodontal care is a critical component to enable long-term success. Further, due to the complexity, case instability and loss of function, option zero (no treatment) is rarely an option.

## R5.2 | How relevant is tooth retention?

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| Additional question raised by the WG  |
| R5.2 - Expert consensus-based recommendation  |
| <i>We <b>recommend</b> tooth retention to be the first line of treatment strategy in the rehabilitation of stage IV periodontitis patients.</i> |
| <b>Supporting literature</b> (Montero et al., 2021; Tomasi et al., 2021)  |
| <b>Quality of evidence</b> Low  |
| <b>Grade of recommendation</b> Grade A – ↑↑   |
| <b>Strength of consensus</b> Strong Consensus (0% of the group abstained due to potential Col)  |

### Background

In the long-term management of stage IV periodontitis, retention of the natural dentition with adequate therapy, whenever possible, provides a strategic advantage as it defers the time and shortens the required longevity of implant-based options. The option of tooth retention needs to be considered first and alternatives need to be justified for the specific case based on case and individual tooth prognosis, technical feasibility, patient preference and, ideally, cost-benefit considerations.

## R5.3 | How relevant is preservation of dental arch integrity

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| Additional question raised by the WG   |
| R5.3 - Expert consensus-based recommendation   |
| <i>In patients with stage IV periodontitis, we <b>suggest</b> preserving the integrity of the dental arch by avoiding extractions, if teeth can be retained.</i> |
| <b>Supporting literature</b> Expert opinion  |
| <b>Quality of evidence</b> Not applicable  |
| <b>Grade of recommendation</b> Grade B – ↑   |
| <b>Strength of consensus</b> Consensus (0% of the group abstained due to potential Col)  |

### Background

In cases with an intact dental arch (no missing teeth apart from the molar area), the possibility to preserve all teeth and thus avoid the need for tooth replacement through periodontal and/or restorative treatment provides a strategic advantage. It may simplify treatment and reduce costs. A careful diagnosis of the possibility to preserve “hopeless” or severely compromised teeth by advanced periodontal therapy, combined with management of hypermobility and/or addressing patient concerns, should be performed before deciding to extract teeth in such cases.

**R5.4 | Can acceptability of tooth preservation be improved with simple measures?**

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| <b>Additional question raised by the WG</b>  |
| <b>R5.4 – Expert consensus-based recommendation</b>  |
| <i>In patients with stage IV periodontitis requesting improvement of aesthetics, phonetics, masticatory function, and/or patient well-being, direct and indirect tooth restorations and/or epitheses <b>may be considered.</b></i> |
| <b>Supporting literature</b> Expert opinion  |
| <b>Quality of evidence</b> Not applicable  |
| <b>Grade of recommendation</b> Grade O - ↔   |
| <b>Strength of consensus</b> Consensus (0% of the group abstained due to potential Col)  |

**Background**

In many stage IV periodontitis cases, the aesthetic, phonetic and functional sequelae of periodontal breakdown severely impact patient well-being and quality of life. Once correctly identified, such concerns may raise questions on tooth-retention based choices, unless costly approaches are considered, and may provide barriers to the acceptability of periodontal therapy and tooth retention. Simple approaches, such as the use of gingival epitheses (custom made removable silicone masks to replace missing gingiva that hide black triangles or correct the presence of uneven gingival margins) and/or direct/indirect adhesive restoration that reshape teeth (and sometimes provide a splinting effect) may mitigate patient concerns and increase the acceptability of periodontal treatment in stage IV periodontitis patients.

## 6 | CLINICAL RECOMMENDATIONS – CASE TYPE 1

***Case type 1 - the patient with tooth hypermobility and secondary occlusal trauma that can be corrected without tooth replacement***

### 6.1 | Intervention – Tooth splinting and occlusal adjustment in patients with periodontitis stage IV

A systematic review (Dommisch et al., 2021) assessed the efficacy of tooth splinting (TS) and occlusal adjustment (OA), compared to no TS or OA in patients with periodontitis exhibiting masticatory dysfunction. Both treatment modalities are especially relevant in fully dentate patients with stage IV periodontitis. In this context, TS reduces tooth mobility due to advanced attachment loss to facilitate biting and chewing abilities (patient’s comfort), and OA addresses secondary occlusal trauma in the management of occlusal dysfunction. In the systematic review (Dommisch et al., 2021), no study specifically focused on patients with stage IV periodontitis, and thus, the efficacy of TS and OA was evaluated for patients with all stages of periodontitis.

The primary outcome criterion was tooth loss (TL), and the secondary outcome parameters were change in probing pocket depth (PPD), change in clinical attachment level (CAL), tooth mobility (TM), and patient-reported outcome measures (PROMs) (Dommisch et al., 2021). For TS, two studies were included considering a follow-up time range between 3-15 and 2-32.4 years, respectively. Three studies addressed OA with a follow up of 2-8 years.

**R6.1 | In fully dentate patients with periodontitis stage IV with increased tooth mobility due to advanced periodontal attachment loss, what is the effectiveness of tooth splinting and/or limited occlusal adjustment of hypermobile teeth?**

***(Common question for Recommendations R6.1, R6.2)***

PICOS question addressed by a SR

R6.1 - Evidence-based recommendation

*In patients with stage IV periodontitis, temporary splinting and/or limited selective occlusal adjustment of hypermobile teeth **may be considered** during all steps of*

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| <i>periodontal therapy (but particularly during step 1 treatment) to increase patient comfort and enable/facilitate periodontal therapy.</i> |
| <b>Supporting literature</b> (Dommisch et al., 2021; Sonnenschein, Ciardo, et al., 2021; Sonnenschein, Ziegler, et al., 2021)                |
| <b>Quality of evidence</b> Very low  |
| <b>Grade of recommendation</b> Grade O - ↔   |
| <b>Strength of consensus</b> Unanimous Consensus (0% of the group abstained due to potential Col)  |

## Background

### Intervention

TS and OA in fully dentate patients with periodontitis.

### Available evidence

#### *Number and design of included studies*

For **Tooth Splinting**, the two included retrospective studies (n=72 patients) analysed a time follow-up time-period ranging between 2 to 32.4 years. After a minimum of 2 years following non-surgical periodontal therapy, synthesis of data revealed a weighted mean incidence of 8.4% TL for tooth splinting compared to 10.1% TL for no-tooth splinting. Outcome measures comprised, beside TL, PPD, change in CAL, change in bone level (BL), and plaque scores. Biological complications, PROMs, health economic parameters and adverse events were not consistently reported.

One additional randomized prospective study indicated a positive effect on the oral health-related quality of life three months after non-surgical periodontal therapy (Sonnenschein, Ziegler, et al., 2021). The timepoint of splinting (prior or following step 2 of periodontal therapy) was addressed in a randomized trial, and the timing appeared not to influence the outcome of periodontal parameters (Sonnenschein, Ziegler, et al., 2021).

Throughout periodontal therapy, splint repairs were frequently required (Graetz et al., 2019; Sonnenschein et al., 2017). In patients with periodontitis stage IV, both tooth splinting and advanced attachment loss may widely impair the patient's aesthetics.

The main findings were that tooth TS does not affect tooth loss, and does not affect PPD, CAL, and BL.

Finally, and in preparation for step 3 of periodontal therapy, since an increase of tooth mobility following flap mobilization is anticipated, tooth splinting may be beneficial when regenerative periodontal treatment is planned (Cortellini et al., 2001).

For **Occlusal Adjustment**, three studies (n=205 patients) were included, one randomized controlled clinical trial (RCT) (Burgett et al., 1992) and two prospective studies (randomization did not include OA procedures) (Fleszar et al., 1980; Kerry et al., 1982). All studies were of prospective design. While two studies included OA as part of the initial phase, one study allocated OA randomly facilitating a comparison of patients with and without OA and no-OA. The follow-up time ranged from 2 to 8 years. None of the studies reported on TL or PROMs. The main findings were that the effects of OA on TL are unclear, that OA positively affects CAL, and that OA does not affect PPD and BL.

#### *Risk of bias*

For TS, study quality assessment using the Newcastle-Ottawa scale identified a low risk of bias for both studies included. For OA, study quality assessment using the Cochrane Collaboration's tool for assessing risk of bias identified unclear risk of bias, mainly related to potential centre bias.

#### *Effect sizes and their clinical relevance*

For **TS**, based on two retrospective case series (n=72 patients), over at least 2 years mean TL was 8.4% for TS and 10.1% for no-TS. TS may be performed as an adjunctive intervention for teeth with a progressive increase in tooth mobility in order to improve the patient's chewing capabilities.

For **OA**, based on one study (n=50 patients), CAL was monitored over a period of 2 years (Burgett et al., 1992). After 1 and 2 years, occlusal adjustment led to an improved CAL of approximately 0.4 mm (mean) following non-surgical periodontal therapy. Although this improvement may not be considered as clinically relevant, occlusal adjustment may remove jiggling forces, facilitate patients' chewing capabilities and resolve pain perception when premature contacts are removed.

#### *Consistency*

In the analysis of **TS**, only two articles exhibiting heterogenous data with a wide range of follow-up examinations (between 2 to 32.4 years) were in accordance with the inclusion criteria of the systematic review. The included studies differed regarding the definition of the control group as well as operators performing splinting and periodontal examination. In addition, one study reported a high dropout rate (Sonnenschein et al., 2017).

In the analysis of **OA**, only three studies of heterogeneous design were in accordance with the inclusion criteria of the systematic review. Of these three studies, one study was designed as an RCT focusing on randomization for OA (Burgett et al., 1992), while the two remaining studies randomised for periodontal treatment modalities but not for OA (Fleszar et al., 1980; Kerry et al., 1982).

#### *Balance of benefit and harm*

For **TS**, the overall evidence suggests a very weak positive relationship between benefit and harm/risks. Although TS does not improve tooth survival, a positive effect on the individual patient comfort exists. However, if TS is performed, splinting technique, material and design should enable optimal self-performed and professional oral hygiene procedures.

Preliminary data exists on oral health related quality of life (OHRQoL) in periodontitis patients. Three months after non-surgical periodontal therapy, a positive impact on the OHIP-14 summary scores was documented suggesting a trend towards improved patients' comfort (Sonnenschein, Ziegler, et al., 2021). There is a lack of information on PROMs and adverse events, and those need to be evaluated in future research.

For **OA**, the existing evidence suggests a weak positive relationship between benefit and harm/risks. There is no information on PROMs and adverse events, and those need to be evaluated in future research.

#### Overall certainty of the evidence

Very low for both TA and OA.

#### From evidence to recommendation- additional considerations

##### *Acceptability*

The certainty of evidence is graded as very low based on the lack of studies, study design and lack of generalizability of data.



### Feasibility

Both, TS and OA can be performed by general dentist as well as specialist as the minimum standard of care.

### Ethical Considerations

Based on the available evidence, no evaluation of ethical aspects could be performed. TS *per se* is a minimal-invasive, and in most cases, reversible therapeutic procedures that does not negatively influence tooth survival. OA is a minimal-invasive but not reversible therapeutic procedure that does not negatively influence periodontal outcome variables.

### Economic Considerations

Health-economic parameters were not evaluated in the identified studies.

### Legal Considerations

Not applicable.

## R6.2 | See question for R6.1

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| PICOS question addressed by a SR  |
| R6.2 - Evidence-based recommendation  |
| <i>In patients with stage IV periodontitis who do not require tooth replacement but show persistent hypermobility or increasing mobility after successful completion of periodontal therapy, long-term tooth splinting <b>may be considered</b> to improve patient comfort.</i> |
| <b>Supporting literature</b> (Dommisch et al., 2021; Sonnenschein, Ciardo, et al., 2021; Sonnenschein, Ziegler, et al., 2021)   |
| <b>Quality of evidence</b> Very low   |
| <b>Grade of recommendation</b> Grade O - ↔  |
| <b>Strength of consensus</b> Unanimous Consensus (0% of the group abstained due to potential Col)   |

### Background

See the background text for Recommendation R6.1.

## **7 | CLINICAL RECOMMENDATIONS – CASE TYPE 2**

***Case type 2 - the patient with pathological tooth migration, characterised by tooth elongation, drifting and flaring, which is amenable to orthodontic correction***

### **7.1 | Introduction - treatment of pathological tooth migration in stage IV periodontitis patients**

Stage IV periodontitis is characterized by similar severity and complexity as stage III periodontitis in terms of periodontal inflammation, attachment and bone loss, but these stage IV periodontitis patients present in addition one or more of the following criteria:

- Loss of more than four teeth that can be attributed to periodontitis.
- Tooth migration, drifting, spacing associated with severe attachment loss at the affected teeth.
- Loss of posterior support and/or flaring of anterior teeth consequent to periodontitis.
- Secondary occlusal trauma/tooth hypermobility attributable to reduced periodontal attachment consequent to periodontitis.
- Loss of masticatory function (masticatory dysfunction) secondary to a combination of the above.

Common to these patients is that the lack of appropriate treatment, not only risks the loss of affected teeth, but of the whole dentition. In stage IV periodontitis patients the treatment of periodontitis (through standard periodontal therapy, i.e., steps I-III plus supportive periodontal care) is not enough to stabilize the case, resolve the masticatory dysfunction and improve their quality of life. An interdisciplinary treatment plan, therefore, must be implemented, which may include orthodontic and/or prosthetic rehabilitation for the stabilization and/or restoration of the masticatory function, patient esthetics and quality of life.

In stage IV periodontitis patients, there are specific phenotypic variations/clinical scenarios based on the individual patterns of the periodontal breakdown, which result in different

degrees of functional and aesthetic compromise, as well as in different treatment needs. One of the most common phenotypic variations is the clinical case defining the patient with pathological tooth migration, characterised by tooth elongation, drifting and flaring, which is amenable to orthodontic correction. This consensus report presents the evidence-based and expert-based recommendations of the present clinical practice guideline for the treatment of the described case type (type 2) of stage IV periodontitis (Figure 2).

Therefore, recommendations refer to combined periodontal and orthodontic treatment in stage IV periodontitis patients where orthodontic therapy is indicated.

## 7.2 | Clinical recommendations for case type 2 - Orthodontic therapy in the treatment of stage IV periodontitis patients

### R7.1 | In stage IV periodontitis patients, when there is an indication for both periodontal and orthodontic therapy, what is the effect of orthodontic therapy (OT) on periodontal health and what are the possible adverse effects and complications?

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| PICOS question addressed by a SR  |
| R7.1 - Evidence-based recommendation  |
| <i>In successfully treated stage IV periodontitis patients in need of orthodontic treatment, we <b>suggest</b> undertaking OT based on evidence that:</i> |
| <i>a) it does not significantly affect periodontal outcomes (probing pocket depth-PPD and clinical attachment levels-CAL).</i>                            |
| <i>b) it does not significantly affect gingival inflammation (bleeding on probing-BOP) and gingival recession.</i>  |
| <i>c) it does not lead to a significant increase in root resorption.</i>  |
| <b>Supporting literature</b> (Martín et al., 2021)  |
| <b>Quality of evidence</b> Moderate   |
| <b>Grade of recommendation</b> Grade B – ↑  |
| <b>Strength of consensus</b> Consensus (0% of the group abstained due to potential CoI)   |

## Background

### Intervention

Treated Stage IV Periodontitis patients frequently require orthodontic therapy (OT) to restore the tooth position and functional occlusion, which during the progression of periodontitis have pathologically migrated, as consequence of periodontal attachment and bone loss. In these patients with a healthy but reduced periodontium, the results of OT may be different, compared to patients without attachment loss, or the orthodontic tooth movements may cause adverse effects on the affected teeth or on the remaining periodontium.

### Available evidence

#### *Number and design of included studies*

The SR by Martín et al. (Martín et al., 2021) included 35 studies. These studies were mainly case series with a pre-post design (15 prospective and 5 retrospective) or cohort studies (4 prospective and 2 retrospective) evaluating the outcomes of OT in periodontitis patients; or studies comparing the outcomes of OT between periodontitis versus non periodontitis patients, either with RCTs (1 split mouth and 7 with parallel arms), or CCT (1 split mouth).

#### *Risk of bias*

The overall quality of the included studies was evaluated as “low.” From the eight RCTs assessed using ROB 2.0 tool, the overall bias assessment was rated as “high” for 2 RCTs; as “low risk of bias” for 3 RCTs and as “some concern” in the other 3. Regarding the 20 pre-post intervention studies, only 1 was rated as “good” quality, 10 was rated as “fair” (moderate risk of bias) and 9 as “poor”. The cohort studies were rated with the Newcastle Ottawa Scale (NOS) scale with 4 being rated as “fair” quality, one as “poor” and one as “good”.

#### *Effect sizes and clinical relevance*

##### *A. Periodontal outcomes (PPD and CAL)*

In patients without periodontitis, changes in CAL (mm) (mean effect - ME=0.248; 95% confidence interval -CI [-0.055; 0.551]; p=0.109) were minimal and non-statistically significant across time (p>0.05). For changes in PPD (mm), a statistically significant reduction was observed (ME=0.325; 95% CI [0.123; 0.526]; p<0.001).

In patients with treated periodontitis, no significant changes were observed in CAL (mm) (ME=0.202; 95% CI [-0.018; 0.422]; p=0.072). There was a slight reduction in PPD (mm) (ME=0.129; 95% CI [0.058; 0.200]; p<0.001), during orthodontic therapy.

#### *B. Gingival inflammation and gingival recession*

In patients without periodontitis, changes in BOP (%) (ME=3.63; 95% CI [-2.11; 9.37]; p=0.215) and in gingival recession (REC) (mm) (ns=2, np=26; ME=0.23; 95% CI [-0.32; 0.77]; pp=0.418) were minimal and non-statistically significant (p>0.05).

In patients with treated periodontitis, also changes in BOP (%) (ME=0.96; 95% CI [-0.77; 2.69]; p=0.278) or REC (mm) (ME=0.08; 95% CI [-0.37; 0.53]; p=0.731) were minimal during orthodontic therapy and not statistically significant.

#### *C. Root resorption*

Due to the scarcity of the data, no meta-analyses could be constructed for adverse effects. The advent of root resorption after the orthodontic treatment in periodontitis patients was reported in a few studies irrespective of the type of orthodontic movement or anchorage system used. In the conventional anchorage group, one study (Melsen, Agerbaek, & Markenstam, 1989) reported 1 to 3 mm of root resorption when the incisors were orthodontically intruded, while in another study (Corrente, Abundo, Re, Cardaropoli, & Cardaropoli, 2003) no resorption using similar orthodontic movements was reported. In the skeletal anchorage group, only one study reported apical root resorption (ranging from 0.2 to 0.4 mm) in the periodontally treated group, while similar root resorption was also reported in periodontally healthy patients treated by OT (ranging from 1 to 1.5 mm).

#### *Balance of benefit and harm*

OT has no detrimental effects on periodontal conditions in periodontitis patients with a healthy but reduced periodontium, provided the orthodontic tooth movements are carried out in teeth without significant gingival inflammation. Overall, the benefits exceed the potential harms.

#### *Consistency*

All studies reported the same tendency.

#### *Overall certainty of the evidence*

The evidence was graded as moderate since a relevant number of studies reported consistent results, albeit with moderate to high risk of bias.

*From evidence to recommendation- additional considerations*

*Acceptability*

Considering the likely benefits (improved tooth position, functional occlusion, and aesthetics) this treatment is well accepted by the patients, although there is lack of evidence on patient reported outcomes (PROMs) from the referred studies.

*Feasibility, ethical and economic considerations*

Considering that OT in patients with a reduced periodontium may be a complex treatment frequently requiring application of complicated devices and appliances, what requires that appropriate specialists or dentists with advanced training implement these treatments. Furthermore, these orthodontic treatments are usually long and require regular visits, what imposes the patient or the health system with considerable costs. There are, however, no available cost effectiveness studies for these combined perio-ortho treatments. The considerable costs needed for these treatments are mainly financially supported by the affected individuals in many European countries, what may result in inequity when not healthcare funding is available. Furthermore, the availability for appropriate professionals to render these complex treatments may vary widely.

*Legal Considerations*

There are usually no legal constraints to OT.

**R7.2 | In stage IV periodontitis patients, when should orthodontic therapy (OT) start?**

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| <b>Additional question addressed by the WG</b>   |
| <b>R7.2 - Expert consensus-based recommendation</b>  |
| <i>In successfully treated stage IV periodontitis patients in need of orthodontic treatment, we <b>recommend</b> starting OT once the endpoints of periodontal therapy have been achieved [no sites with PPD=5 mm and BOP and no sites with PPD≥6 mm (Sanz, Herrera, et al., 2020)].</i> |
| <b>Supporting literature</b> Expert opinion; data from preclinical studies   |

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| <b>Quality of evidence</b> Low (expert opinion)  |
| <b>Grade of recommendation</b> Grade A – ↑↑  |
| <b>Strength of consensus</b> Strong consensus (0% of the group abstained due to potential Col) |

## Background

### Intervention

Orthodontic Therapy (OT) is indicated for the functional and aesthetic rehabilitation of stage IV periodontitis patients with pathological tooth migration, characterised by tooth elongation, drifting and flaring. This orthodontic therapy must fulfill its objectives without jeopardizing the outcomes of periodontal therapy and hence it is important to stage it appropriately within the overall patient's treatment plan.

### Available evidence

#### *Number and design of included studies*

The evidence for this recommendation is derived from expert opinion and from experimental *in vivo* investigations.

#### *Risk of bias*

Not applicable.

#### *Effect sizes and their clinical relevance*

The evidence derives from well controlled preclinical *in vivo* investigations (Eliasson, Hugoson, Kurol, & Siwe, 1982; Ericsson, Thilander, Lindhe, & Okamoto, 1977; Melsen, 1986; Wennstrom, Stokland, Nyman, & Thilander, 1993) clearly indicating that when periodontitis is not fully treated (inflammation is not arrested) prior / during orthodontic treatment, these orthodontic (biomechanical) forces within the periodontal tissues with remaining inflammatory processes will accelerate the progression of periodontal destruction, leading to further loss of clinical attachment and bone. In contrast, no detrimental effects of orthodontic tooth movements have been observed when these movements affect teeth with healthy (non-inflamed) reduced periodontal support.

### *Consistency*

All the referred pre-clinical investigations report consistent results indicating that when periodontitis is not adequately controlled, OT will result in further tissue destruction, evidenced by loss of periodontal attachment and alveolar bone.

### *Balance of benefit and harm*

These unwanted effects (further loss of periodontal attachment and bone) clearly outweigh the benefit of OT and hence, orthodontic tooth movements should not be started until periodontal inflammation is arrested, when fulfilling the well-established end points of periodontal therapy (Sanz, Herrera, et al., 2020).

### *Overall certainty of the evidence*

Low, expert opinion.

### *From evidence to recommendation- additional considerations*

#### *Acceptability*

Patients usually accept and understand, once they have been explained the balance of the associated benefits versus harms, that OT can only be implemented once periodontal therapy has been completed and the end points of periodontal therapy have been reached.

#### *Feasibility, ethical and economic considerations*

The only perceived barrier is the length of overall treatment, but since the risks clearly outweigh the benefits, this barrier is usually well accepted.

There are no ethical or economic considerations.

#### *Legal considerations*

There are no legal considerations.

## **R7.3 | How should we manage stage IV periodontitis patients with pathological tooth migration (flaring, drifting and, elongation)?**



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| PICOS question addressed by a SR   |
| R7.3 - Evidence-based recommendation   |
| <i>In stage IV periodontitis patients with pathological tooth migration, we <b>suggest</b> undertaking orthodontic therapy once the endpoints of periodontal therapy have been reached, based on the evidence that this therapy:</i> |
| <i>a) does not significantly affect periodontal outcomes [CAL, PPD, and radiographic bone levels (RBL)]</i>  |
| <i>b) seems to reduce gingival inflammation (BOP)</i>  |
| <i>c) does not significantly alter gingival margin levels</i>  |
| <i>d) seems to improve interdental papilla height</i>  |
| <i>e) does not significantly affect root resorption and seems to reduce tooth mobility.</i>  |
| <b>Supporting literature</b> (Papageorgiou et al., 2021)   |
| <b>Quality of evidence</b> Moderate  |
| <b>Grade of recommendation</b> Grade B – ↑   |
| <b>Strength of consensus</b> Consensus (0% of the group abstained due to potential Col)  |

## Background

### Intervention

Pathological tooth migration is a frequent sequela of periodontal attachment loss in stage IV periodontitis patients manifested by tooth drifting, flaring and elongation. Its correction requires OT after completion of periodontal therapy. The orthodontic treatment of these sequelae usually involves intrusive, retrusive, and alignment tooth movements, which may potentially cause adverse effects (further periodontal attachment or bone loss, increased gingival inflammation, or increased root resorption) or secondary effects (undesired aesthetic outcomes such as gingival recession and loss of interdental papilla) to the affected teeth.

### Available evidence

#### *Number and design of included studies*

Thirty-four studies (from thirty-seven publications) were included, reporting data from 1090 participants with mean age of 43.7 years and a gender ratio (female/male) of 3/1. Included studies were either comparative (randomized or non-randomized) or single-group cohort

studies with at least one group with pre-post data combining periodontal-orthodontic treatment in stage IV periodontitis patients with pathologic tooth migration.

Data were analyzed either directly from comparative studies (randomized/non-randomized) or indirectly by pooling all study arms from pre-post data studies calculating the average effects for each outcome and identifying the associated factors through subgroup/meta-regression analyses. Data for periodontal outcomes was retrieved from two comparative studies for PPD and from one study for RBL. Indirect meta-analyses from single-group before-and-after studies assessed CAL (7 studies), PPD (7 studies) and RBL (7 studies). Gingival inflammation was reported in one retrospective non-randomized comparative study, while gingival recession was reported in 3 non-randomized single-group before-and-after studies. Interdental papilla height by indirect meta-analysis from 2 non-randomized single-group before-and-after studies and root resorption by indirect meta-analysis from 3 non-randomized single-group before-and-after studies.

#### *Risk of bias*

All studies were evaluated as high risk of bias based on the ROBINS-I or ROB 2.0 tools.

#### *Effect sizes and their clinical relevance*

There was no statistically significant difference in the overall PPD change between combined periodontal-orthodontic treatment compared to periodontal therapy alone (meta-analysis of 2 non-randomized multi-group comparative cohort studies with 92 patients [MD=-0.31 mm; 95% CI=-0.83 to 0.22 mm; P=0.26; I<sup>2</sup>=83%]).

Indirect analyses from single-group before-and-after studies on the effect of orthodontic treatment reported significant CAL-gain with a pooled change=-0.24 mm (95% CI=-0.38 to -0.10 mm; P<0.001; I<sup>2</sup>=79% [7 studies]). Similarly, there was PPD reduction with a pooled change=-0.23 mm (95% CI=-0.49 to 0.04 mm; P=0.09; I<sup>2</sup>=95% [7 studies]); and RBL gain with a pooled change=-0.36 mm (95% CI=-0.59 to -0.13 mm; P=0.002; I<sup>2</sup>=88% [7 studies]).

There was no significant effect in terms of %RBL changes from the combined periodontal-orthodontic treatment (1 study; 20 patients; MD=-0.60%; 95% CI=-2.80 to 1.60%; P=0.59).

One study reported reduced *gingival inflammation* (bleeding index) with combined periodontal-orthodontic treatment compared to only periodontal treatment (1 study; 72 patients; MD=-13.89%; 95% CI=-16.06 to -11.72%; P<0.001).

Indirect meta-analyses reported no significant effect on average gingival recession either for the combined periodontal-orthodontic treatment with pooled change=-0.53 mm (95% CI=-2.07 to 1.01 mm; P=0.50; I<sup>2</sup>=98% [3 studies]); or solely for the orthodontic treatment subsequent to periodontal therapy, with pooled change=0.09 mm (95% CI=-0.01 to 0.20 mm; P=0.09; I<sup>2</sup>=0% [2 studies]).

Indirect meta-analysis reported increased interdental papilla height after orthodontic treatment with pooled change=-1.42 mm (95% CI=-1.98 to -0.86 mm; P<0.001; I<sup>2</sup>=94% [2 studies]).

Indirect meta-analyses reported no significant increase in root resorption either for the combined periodontal-orthodontic treatment with pooled change=-0.42 mm (95% CI=-0.63 to -0.22 mm; P<0.001; I<sup>2</sup>=56% [3 studies]); or solely for the subsequent orthodontic treatment with pooled change=-0.49 mm (95% CI=-1.04 to 0.06 mm; P=0.08; I<sup>2</sup>=71% [2 studies]).

### *Consistency*

The results on the periodontal outcomes and gingival inflammation indicated either minor non-relevant effects or benefits from the combined periodontal-orthodontic treatment. Consistency could not be formally assessed by direct meta-analysis due to the small number of included studies.

### *Balance of benefit and harm*

In these patients the benefit after OT clearly outweighs the harm since the overall pooled effect resulted in a beneficial impact on CAL, PPD, RBL and gingival inflammation without being associated with significant adverse or secondary effects.

### *From evidence to recommendation- additional considerations*

#### *Acceptability*

The addition of orthodontic therapy might impose an additional burden in patients, but the expected benefits resulting from the improved function and aesthetics are usually

understood and well accepted by the affected patients, although there is lack of evidence on patient reported outcomes (PROMs) from the referred studies.

*Feasibility, ethical and economic considerations*

These combined treatments need the collective effort of many oral health providers (dental hygienists, periodontists, orthodontists or dentists with advanced training and skills) since beyond the management of the orthodontic therapy, patient’s oral hygiene and periodontal status must be carefully monitored throughout the treatment. Availability of these needed human resources vary widely depending on the environment and may be influenced by the available public healthcare funding, since in many instances it must be self-funded by the affected patient, what may implicate inequalities in the access to these treatments. There is no evidence on the economic effects, since there are no cost-effectiveness studies, although these combined periodontal/orthodontic treatments are usually costly since they require complex interventions and require multiple care providers.

*Legal considerations*

There are no apparent legal constraints.

**R7.4 | How should we manage stage IV periodontitis patients with tilted molars?**

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| PICOS question addressed by a SR  |
| R7.4 - Expert consensus-based statement   |
| <i>In stage IV periodontitis patients with tilted molars orthodontic therapy <b>may be considered</b>, although there is a lack of evidence on its possible effect on periodontal outcomes.</i> |
| <b>Supporting literature</b> (Kloukos et al., 2021)   |
| <b>Quality of evidence</b> Very low   |
| <b>Grade of recommendation</b> Grade O - ↔  |
| <b>Strength of consensus</b> Strong consensus (0% of the group abstained due to potential Col)  |

**Background**

Intervention

Tilted molars are a frequent sequela of tooth loss and periodontal attachment loss in stage IV periodontitis patients, often in combination with bite collapse and loss of the vertical dimension of the occlusion. The treatment of these sequelae usually involves OT using movements of tooth up-righting, what may cause adverse effects to the affected teeth (further attachment and/or bone loss).

### Available evidence

#### *Number and design of included studies*

The SR by (Kloukos et al., 2021) has only identified 1 study evaluating the effect of OT on tilted molars (Kraal, Digiancinto, Dail, Lemmerman, & Peden, 1980). This split- mouth retrospective study reported a single cohort of patients, where in one side tilted molars were orthodontically treated, while in the contralateral side, they were not.

#### *Risk of bias*

Using the ROBINS-I-tool, this study by Kraal et al. (Kraal et al., 1980) was rated as of critical risk of bias.

#### *Effect sizes and their clinical relevance*

There was no data available on PPD or CAL changes. Results only reported mean radiographic bone height changes. In 15 patients with treated and untreated sides, mean bone height change was -2.21 mm (SD=4.53) in untreated, versus -1.07 mm SD=7.35) in treated teeth. The mean bone height change was -2.53 mm (SD=4.53) in 15 untreated molars, versus -1.60 mm (SD=7.01) in 21 up righted molars. Due to the scarcity of available evidence the clinical relevance of these results could not be considered.

#### *Balance of benefit and harm*

Adverse effects such as tooth loss, abscess, or decay were not reported in this study. Similarly, success and duration of orthodontic tooth movement, as well as subjective/objective evaluation of masticatory function or PROMs were not reported. Due to the scarcity of available evidence the balance of benefit versus harm of this type of combined perio-ortho therapy could not be assessed.

### Overall certainty of the evidence

Considering the evidence derived from only one retrospective study the overall certainty of the evidence was rated as very low.

### From evidence to recommendation- additional considerations

Acceptability, feasibility, ethical, economic, and legal considerations of this intervention could not be evaluated.

**R7.5 | In stage IV periodontitis patients presenting with intrabony defects and in need of OT, what is the outcome of the combined periodontal and orthodontic therapy and what should be the time interval between the periodontal regenerative and orthodontic therapies?**

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| <b>PICOS question addressed by a SR</b>   |
| <b>R7.5 - Evidence-based recommendation</b>   |
| <i>In stage IV periodontitis patients where intrabony defects have been treated following the recommendations of the clinical practice guideline [(Sanz, Herrera, et al., 2020) using the appropriate regenerative interventions]:</i> <ol style="list-style-type: none"><li><b>we recommend</b> undertaking OT based on the evidence that the combined treatment significantly improves periodontal outcomes (increased CAL gain, PD reduction, and RBL gain) and significantly reduces gingival inflammation (BOP)</li><li><b>we suggest</b> not to wait for a prolonged healing period after the regenerative intervention, before initiating OT, since there is evidence that a short (1 month) and a prolonged (6 months) period between periodontal /regenerative and orthodontic treatment result in comparable outcomes</li></ol> |
| <b>Supporting literature</b> (Kloukos et al., 2021; Martín et al., 2021; Papageorgiou et al., 2021)   |
| <b>Quality of evidence</b> Moderate   |
| <b>Grade of recommendation</b> Grade A - ↑↑ (1); Grade B – ↑ (2)  |
| <b>Strength of consensus</b> Consensus (10.6% of the group abstained due to potential Col)  |

### **Background**

#### Intervention

Teeth with intrabony defects are frequently present in stage IV periodontitis patients. These defects are not only a complexity factor for the periodontal therapy but may also affect the

outcomes of orthodontic therapy since tooth movements may occur through the regenerated tissues. As reported in the previously published S3-Level CPG of periodontal treatment for stage I-III periodontitis patients (Sanz, Herrera, et al., 2020), these intrabony defects should be treated during the step 3 of periodontal therapy by surgical periodontal regenerative interventions. After this therapy it is relevant to understand whether orthodontic tooth movements can be implemented safely in these affected teeth, and what is the appropriate time interval between the surgical intervention and the start of active orthodontic tooth movements.

### Available evidence

#### *Number and design of included studies*

Data from the three SRs (Kloukos et al., 2021; Martín et al., 2021; Papageorgiou et al., 2021) were retrieved from 16 studies including a total number of 683 patients: being 3 RCTs, 10 prospective and 3 retrospective case series studies.

#### *Risk of bias*

Using the Risk of Bias 2.0. tool, 2 RCTs were rated high risk of bias. The RCT comparing early versus delayed orthodontic treatment (Jepsen et al., 2021) was rated low risk of bias. The remaining 13 studies, using the ROBINS-I-tool. were rated as critical risk of bias in 8 studies, as serious risk of bias in 4, and as fair risk in 1 study.

#### *Effect sizes and their clinical relevance*

Twelve studies reported on mean PPD changes in mm, while in 1 study the mean PPD changes were reported in percentages. Outcomes from 2 RCTs indicated a PPD reduction of  $2.17 \pm 0.20$  mm and  $4.21 \pm 1.35$  mm, respectively, while the results from non-RCTs indicated mean PPD changes ranging from  $-0.07 \pm 0.75$  mm to  $-5.5 \pm 1.5$  mm. A retrospective cohort study with 48 patients (Tietmann, Broseler, Axelrad, Jepsen, & Jepsen, 2021), reported a mean PPD reduction of 2.5 mm and a mean RBL gain of 4.7 mm after 12 months. Pocket closure (PPD  $\leq$  4 mm) was attained in 87 % of defects.

Mean CAL changes were reported in 8 studies. In 2 RCTs, CAL change was  $3.09 \pm 0.47$  mm and  $3.67 \pm 0.76$  mm, respectively, while in non-RCTs CAL change ranged from  $0.29 \pm 0.17$

mm to  $5.93 \pm 1.41$  mm. The results from the RCT comparing orthodontic therapy starting early versus late after the periodontal regenerative intervention demonstrated a potential beneficial effect of the early orthodontic treatment since no statistically significant differences were observed in terms of CAL gain ( $5.4$  mm [ $\pm 2.1$  mm] for early;  $4.5$  mm [ $\pm 1.7$  mm] for late OTM or PPD reduction [ $4.2$  mm ( $\pm 1.9$  mm) in the early group versus  $3.9$  mm ( $\pm 1.5$  mm) in the late group ( $p > 0.05$ )]. Similarly, pocket closure (PPD  $\leq 4$  mm) occurred in 91% of the early OTM treated teeth versus 85% in late (Jepsen et al., 2021).

### *Consistency*

There was general agreement among included studies that in patients with severe periodontitis (stage IV equivalent) and presence of intrabony lesions, the combination of periodontal regenerative treatment with orthodontic therapy positively influenced the periodontal outcomes.

### *Balance of benefit and harm*

Five articles reported on harms/adverse effects. No significant adverse effects were reported. Furthermore, the benefits of early orthodontic therapy (similar outcomes with significantly reduced overall treatment time) seem to outweigh the potential risks.

### *From evidence to recommendation- additional considerations*

#### *Acceptability*

Although there is no evidence from PROMs, the combination of periodontal and orthodontic therapies was well accepted by the patients.

#### *Feasibility*

The combination of complex periodontal and orthodontic therapies requires the coordinated efforts of different oral care providers (specialists or dentists with advanced training and skills in periodontal and orthodontic therapies) and these special settings may not be encountered in every oral health care environment.

#### *Ethical Considerations*

There is no evidence for ethical considerations.



### *Economic Considerations*

There is no evidence from cost-effectiveness studies, although the combined periodontal orthodontic treatment of these patients is complex, requires multiple care providers and it is usually costly.

### *Legal Considerations*

There are no specific legal considerations.

## **R7.6 | How should we implement OT in stage IV periodontitis patients to maintain/improve periodontal outcomes?**

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| <b>PICOS question addressed by a SR</b>  |
| <b>R7.6 - Evidence-based recommendation</b>  |
| <i>In patients with severe periodontitis (stage IV or equivalent) with indication of OT to maintain/improve periodontal stability:</i> <ol style="list-style-type: none"><li><b><i>we suggest</i></b> using fixed rather than removable appliances</li><li>use of fiberotomy as an adjunct to orthodontic tooth movement <b><i>may be considered</i></b> to improve periodontal outcomes</li><li>use of skeletal anchorage devices (implants or TADs – micro-screws or miniplates) <b><i>may be considered</i></b> to enhance orthodontic tooth movement</li></ol> |
| <b>Supporting literature</b> (Martín et al., 2021; Papageorgiou et al., 2021)  |
| <b>Quality of evidence</b> Low   |
| <b>Grade of recommendation</b> Grade B - ↑ (1), Grade O - ↔ (2, 3)   |
| <b>Strength of consensus</b> Consensus (1.7% of the group abstained due to potential Col)  |

## **Background**

### Intervention

- Orthodontic tooth movements can be carried out either by fixed (braces) or removable (able to be inserted /removed by the patients, such as removable plates, thermoplastic aligners, etc.) orthodontic appliances.
- Circumferential fiberotomy of the supragingival periodontal fibers has been suggested as an adjunct surgical procedure to improve the post-treatment stability after correction of

severely rotated teeth or as an intervention aimed to improve attachment levels during orthodontic tooth intrusion.

3. In stage IV periodontitis patients with a healthy but reduced periodontium, the use of skeletal anchorage devices, compared to conventional anchorage systems, may improve the efficacy of OT and its effect on periodontal outcomes.

### Available evidence

#### *Number and design of included studies*

1. One non-randomized retrospective comparative study comparing fixed appliances (braces) with aligners, reporting results from before periodontal to after orthodontic treatment, in terms of CAL/RBL/PPD/root length outcomes.

2 The use of fiberotomy as an adjunct to combined periodontal-orthodontic treatment was assessed in two within-individual RCTs.

3. Anchorage:

- In 4 studies skeletal anchorage (TADs or implants) was used in all patients
- In 12 studies different types of conventional anchorage were used
- 2 studies presented results of patients treated with TADs mixed with patients without TADs.

#### *Risk of bias*

1.Type of orthodontic appliance

The only included study was judged as serious risk of bias using the ROBINS-I tool.

2. Use of fiberotomy

Both randomized trials were judged as high risk of bias using the ROB 2.0 tool for at least two domains each.

3.Anchorage Systems

The overall quality of the included studies was judged as “low.”

- Considering the 12 pre-post intervention studies assessed, 2 were rated as “good”, 4 of them were rated as “fair” (moderate risk of bias) and in 6 was rated as “poor”.
- The study rated according to ROBINS-I tool received an overall assessment of “serious” risk of bias.

- Considering the 5 RCTs assessed using ROB 2.0 tool, the overall bias assessment was “high” for two RCTs; one RCTs was rated as “low risk of bias” and another two were rated with “some concerns”.

### *Effect sizes and their clinical relevance*

1. The included study reported that fixed appliances have benefits over aligners for PPD (1 study; MD=-1.64 mm; 95% CI=-2.50 to -0.78 mm; P<0.001) but not for RBL (1 study; MD=0.01; 95% CI=-1.01 to 1.03; P=0.99).

2. Adjunctive use of fiberotomy was associated with benefits in CAL (1 study; MD=-0.63 mm; 95% CI=-1.10 to -0.16 mm; P=0.009) and RBL (2 studies; MD=-0.98 mm; 95% CI=-1.87 to -0.10 mm; P=0.03), but not PPD (1 study; MD=-0.03 mm; 95% CI=-0.48 to 0.42 mm; P=0.90)

3. In terms of different anchorage systems, there is no evidence of added benefits on periodontal parameters from using a specific type of anchorage system during orthodontic therapy. In terms of orthodontic outcomes, the use of osseointegrated implants as anchorage (one study), TADs (3 studies) and conventional anchorage resulted in different tooth movements (such as intrusion) ranging between 1 and 7 mm, without a clear advantage among the different systems.

Root resorption after the orthodontic treatment in periodontitis patients was reported in studies using different anchorage systems, with similar levels of reported resorption (between 0.2 – 3 mm) with either conventional anchorage or skeletal anchorage. Root resorption was also reported in similar ranges in studies with orthodontic therapy in healthy periodontal patients

### *Consistency*

In relation to the type of orthodontic appliance, since only one study was available, the consistency could not be assessed. For the adjunctive use of fiberotomy, the results were not consistent for the periodontal outcomes. The results using different anchorage systems reported the same tendency.

### *Balance of benefit and harm*

There are no considerable harms with the use of conventional fixed appliances (braces), other than the increased microbial burden, related to the difficulties in oral hygiene practices, which can however be managed appropriately.

Although fiberotomy is a surgical procedure, the possible side effects have not been adequately reported.

There is no evidence of a significant harm associated with the different anchorage systems.

### Overall certainty of the evidence

Low.

### From evidence to recommendation- additional considerations

#### *Acceptability*

1. Some patients might prefer aligners over fixed appliances, due to their enhanced esthetics and easiness for oral hygiene. However, braces have been historically well accepted by adults and there are currently more esthetic alternatives in fixed appliances (ceramic/lingual appliances).
2. Fiberotomy is a surgical intervention, albeit minimally invasive, what might be less acceptable by some patients.
3. Some patients might experience discomfort when receiving TADs, although this fact has not been evaluated in the reported studies.

#### *Feasibility*

1. The use of fixed appliances requires specific knowledge of applied biomechanics, what is usually rendered by orthodontic specialists, while aligners treatment is mostly facilitated through third parties (companies or external laboratories) producing the aligners and enabling both specialists and general dentists to provide this kind of treatment. However, extensive knowledge of tooth biology and applied biomechanics is still a pre-requisite for treatment planning and monitoring.
2. Fiberotomy requires specific surgical experience from the operator.
3. In cases of using skeletal anchorage systems, knowledge of surgical anatomy and surgical skills are needed.

### *Ethical and Economic Considerations*

Fiberotomy as an additional surgical insult to the periodontal tissues must be further evaluated in terms of its long-term effectiveness and since it is an additional surgical intervention, it might be associated with further costs.

### *Legal considerations*

There are no specific legal considerations.

## **R7.7 | How should we manage stage IV periodontitis patients during and after the completion of OT to prevent recurrence of periodontitis?**

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| <b>Additional question addressed by the WG</b>   |
| <b>R7.7 - Expert consensus-based recommendation</b>  |
| <i>We <b>recommend</b> that <u>during</u> OT the patient's periodontal status is closely monitored and managed, ideally at each orthodontic appointment. If signs of periodontitis recurrence are detected, active OT should be interrupted, and the affected teeth should be maintained passively, while rendering proper periodontal treatment and oral hygiene reinforcement. Once periodontal health/stability has been re-established, OT can be re-instituted.</i> |
| <i>We <b>recommend</b> that <u>after</u> completion of OT, life-long supportive periodontal care and life-long orthodontic retention are provided tailored to the individual needs/risk profile of the patient.</i>  |
| <b>Supporting literature</b> Expert opinion, (Arn, Dritsas, Pandis, & Kloukos, 2020; Jiang et al., 2021)   |
| <b>Quality of evidence</b> Low (expert opinion)  |
| <b>Grade of recommendation</b> Grade A – ↑↑  |
| <b>Strength of consensus</b> Unanimous consensus (0% of the group abstained due to potential Col)  |

## **Background**

### Intervention

The use of orthodontic appliances is associated with increased microbial colonization and increased plaque retention; hence, orthodontic treatment is often associated with gingival inflammation and a transient shift of the subgingival microbiota. It is, therefore, important

to implement an appropriate oral hygiene and periodontal management protocol throughout the orthodontic treatment to ensure periodontal health and avoid adverse effects like enamel demineralization, tooth discolorations, and further loss of periodontal support. Although in some patients, an acceptable oral hygiene level can be attained, professional plaque control and other supportive oral and periodontal care must be implemented following the patient's risk profile.

### Available evidence

#### *Number and design of included studies*

The evidence for this recommendation is derived from expert opinion and from a randomized trial with 48 patients comparing three different periodic periodontal scaling protocols (every 1 month, every 3 months, or every 6 months) for oral hygiene in adolescents with fixed orthodontic appliances (Jiang et al., 2021). A systematic review (Arn et al., 2020) assessed the available evidence in the literature for the effects of fixed orthodontic retainers on periodontal health. It included eleven RCTs, 4 prospective cohort studies, 1 retrospective cohort study, and 13 cross-sectional studies.

#### *Risk of bias*

Not applicable.

#### *Effect sizes and their clinical relevance*

One RCT reported that periodontal scaling conducted monthly or once every 3 months during orthodontic treatment was more effective (in terms of PI, GI, PPD and crevicular inflammation biomarkers) than scaling administered once every 6 months. The systematic review concluded that the use of orthodontic fixed retainers was compatible with periodontal health, or at least not associated with detrimental effects on the periodontium. Even though the RCT and the systematic review studied periodontally healthy patients and not to adults with stage IV periodontitis, it is expected that these findings can be reasonably extrapolated.

#### *Consistency, Balance of benefit and harm*

Not applicable.

Overall certainty of the evidence

Low, expert opinion.

From evidence to recommendation- additional considerations

*Acceptability*

Patients usually accept and understand the need for long-term supportive care.

*Feasibility, ethical, economic and legal considerations*

There are no specific considerations.

**R7.8 | How should we attain stability of the orthodontically treated dentition in stage IV periodontitis patients?**

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| <b>Additional question addressed by the WG</b>  |
| <b>R7.8 - Expert consensus-based recommendation</b>   |
| <i>We <b>recommend</b> that an appropriately designed permanent fixed passive retention (with or without additional removable retention) is used after the completion of orthodontic treatment.</i> |
| <i>We also <b>recommend</b> that patients enter a life-long supporting protocol to identify early retainer failures and/or undesired tooth movements.</i>   |
| <b>Supporting literature</b> Expert opinion, (Han et al., 2020)   |
| <b>Quality of evidence</b> Low (expert opinion)   |
| <b>Grade of recommendation</b> Grade A – ↑↑   |
| <b>Strength of consensus</b> Consensus (0% of the group abstained due to potential Col)   |

**Background**

Intervention

Post-orthodontic relapse of the moved teeth towards their pre-treatment positions is often observed and can have aesthetic and functional consequences that compromise treatment outcomes and patient satisfaction. Therefore, some type of retention, either with removable or fixed appliances, is usually implemented depending on the pre-existing malocclusion, the type of tooth movements carried out, and patient preferences. Fixed

retention is usually considered superior to removable appliance in terms of reducing post-treatment relapse, especially in anterior crowding (Littlewood, Millett, Doubleday, Bearn, & Worthington, 2016). However, at the same time it may be more prone to retention failure in the short- or in the long-term, might lead to more plaque accumulation or gingival inflammation, and might even lead to inadvertent tooth movements due to the distortion of the bonded wire. It is, therefore, advisable that fixed retention (with additional removable appliances, if needed) is used after orthodontic treatment in patients with stage IV periodontitis, but a long-term supportive care protocol should be implemented to assess not only periodontal health, but the integrity of the retention appliances and the stability of the treatment outcomes.

#### *Available evidence*

##### *Number and design of included studies*

The evidence for this recommendation is derived from expert opinion and from a retrospective cohort study with 52 patients followed at least 2 years after orthodontic treatment (Han et al., 2020).

##### *Risk of bias*

Not applicable.

##### *Effect sizes and their clinical relevance*

Han et al. (Han et al., 2020) reported that orthodontic fixed retainers fail more often in stage III periodontitis patients compared to stage I periodontitis patients. This study did not include stage IV periodontitis patients, but these findings indicate that increased periodontitis severity was associated with higher retainer failure and hence, in stage IV periodontitis patients, the need for frequent recalls to evaluate the retainer's integrity should be highlighted.

##### *Consistency, Balance of benefit and harm*

Not applicable.



Overall certainty of the evidence

Low.

From evidence to recommendation- additional considerations

*Acceptability*

Patients usually accept and understand the need for long-term fixed passive retention and regular monitoring.

*Feasibility, Ethical, Economic and Legal Considerations*

There are no specific considerations.

## 8 | CLINICAL RECOMMENDATIONS – OVERALL STRATEGY FOR THE MANAGEMENT OF CASE TYPES 3 AND 4

In stage IV periodontitis patients, prosthetic rehabilitation requires adherence to both periodontal and reconstructive treatment principles. Such principles need to be tailored to the specific needs of this patient group. Several key issues need to be addressed, including:

1. Identification of the restorative needs with an emphasis on limiting the scope of the prosthetic treatment while ensuring patient comfort and stability.
2. Identification of the need for interim dental prostheses.
3. Timing of delivery of interim and definitive dental prostheses.
4. Need and timing of dental implant placement.

This section aims to provide recommendations for the general principles of case management in patients with a compromised dentition due to stage IV periodontitis requiring rehabilitation.

### R8.1 | How important is to identify the restorative needs of the individual case in stage IV periodontitis patients?

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| <b>Additional question raised by the WG</b>  |
| <b>R8.1 - Expert consensus-based recommendation</b>  |
| <i>We <b>recommend</b> identifying the restorative needs of partially edentulous stage IV periodontitis patients based on the pattern of tooth loss, individual functional and aesthetic needs, patient comfort and prognostic factors. The level of function and design of the rehabilitation should be compatible with case stability over time.</i> |
| <b>Supporting literature</b> Expert opinion  |
| <b>Quality of evidence</b> Not applicable  |
| <b>Grade of recommendation</b> Grade A – ↑↑  |
| <b>Strength of consensus</b> Strong consensus (0% of the group abstained due to potential Col)   |

#### Background

Stage IV periodontitis cases are characterized by high levels of phenotypic variation. While restorative needs to achieve case stability and address patient comfort are only one dimension of what needs to be considered in treatment planning, precise identification of

these needs is critical. Treatment goals need to be based on the individual patient, its unique pattern of tooth loss, tooth prognosis both in terms of periodontal maintainability and restorative factors. Furthermore, the plan should be able to stop or mitigate greatly the occlusal and functional aspect that contribute to the instability of the case and loss of patient comfort.

**R8.2 | Is there a need, and which is the timing, of interim restorations in stage IV periodontitis patients?**

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| Additional question raised by the WG   |
| R8.2 - Expert consensus-based recommendation   |
| <i>We <b>recommend</b> placing an interim dental prosthesis, if required, early during periodontal therapy, but only after establishing adequate oral hygiene.</i> |
| <b>Supporting literature</b> Expert opinion, (Donos et al., 2021; Montero et al., 2021; Ramanauskaite et al., 2021; Tomasi et al., 2021)                           |
| <b>Quality of evidence</b> Very low  |
| <b>Grade of recommendation</b> Grade A – ↑↑  |
| <b>Strength of consensus</b> Strong consensus (1.9% of the group abstained due to potential Col)   |

**Background**

Once the restorative needs of the case have been identified, interim restorations may be required to provide stable posterior occlusal stops, relieve secondary occlusal trauma, replace functionally important missing teeth, or improve patient comfort. Ideally, the decision to place an interim restoration should be based on the individual response of periodontal therapy as assessed in the periodontal re-evaluation after completion of step 2 treatment. Frequently, the benefits to the treatment plan from interim restorations require their insertion as early as possible. Flexibility to move forward the interim restoration in the treatment plan, however, should not compromise the need to achieve adequate supragingival biofilm control in the context of step 1 treatment.

**R8.3 | Which are the general principles for the design and delivery of dental prostheses in stage IV periodontitis patients?**

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| Additional question raised by the WG         |
| R8.3 - Expert consensus-based recommendation |

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| <i>We <b>recommend</b> designing the dental prostheses to allow optimal self-performed oral hygiene measures and professional mechanical plaque removal.</i> |
| <i>We <b>recommend</b> delivery of the definitive prosthesis after a final evaluation of the maintainability and prognosis of abutment teeth/implants.</i>   |
| <b>Supporting literature</b> Expert opinion, (Donos et al., 2021; Montero et al., 2021; Ramanauskaite et al., 2021; Tomasi et al., 2021)                     |
| <b>Quality of evidence</b> Very low  |
| <b>Grade of recommendation</b> Grade A - ↑↑ / Grade A - ↑↑   |
| <b>Strength of consensus</b> Unanimous consensus (0% of the group abstained due to potential Col)  |

## Background

Oral biofilm control is important for the longevity of the dentition and restorations. This is critically important in subjects with stage IV periodontitis who have shown high susceptibility to periodontitis. Restorations may render access and effectiveness of self-performed biofilm control and professional mechanical plaque removal (PMPR) more challenging. While restorations are primarily designed to restore function, they should enable optimal biofilm control at the critical interface between the restoration, the tooth/root surface, the implant on one side and the soft tissues (gingiva, peri-implant or alveolar ridge mucosa) on the other. Planning and execution of these restorations should preserve the necessary access for oral hygiene aids including interdental brushes or dental floss, as well instruments for PMPR (both supra- and sub-gingivally). This should be prioritized compared to avoidance of food impaction. The design should be finalized with the interim dental prosthesis and achievement of tissue health needs to be verified along with the maintainability of the abutments before insertion of the final prosthesis. Insertion of the final dental prosthesis needs to follow the achievement of the treatment goals for natural teeth and/or implants at the completion of active periodontal therapy.

## R8.4 | Which are the general considerations when incorporating dental implants in stage IV periodontitis patients?

Additional question raised by the WG

R8.4 - Expert consensus-based recommendation

*When dental implants are considered in the rehabilitation of stage IV periodontitis patients, we **recommend** verifying (i) absence of contraindications to surgery, (ii) hard and soft-tissue dimensions and (iii) the potential need for soft/hard tissue augmentation.*

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| <b>Supporting literature</b> Expert opinion   |
| <b>Quality of evidence</b> Not applicable   |
| <b>Grade of recommendation</b> Grade A - ↑↑   |
| <b>Strength of consensus</b> Consensus (3.5% of the group abstained due to potential Col) |

### Background

Dental implants are frequently considered in the rehabilitation of stage IV periodontitis patients to replace missing teeth and restore function. The use of a dental implant, however, may present different levels of complexity and range from a simple procedure in a subject with no medical contraindications and adequate dimensions of soft and hard tissues, to a complex procedure requiring specific medical assessments and/or challenging local hard and/or soft tissue augmentation. As the complexity of the dental implant placement increases, its clinical performance may decrease, affecting the cost-benefit ratio and its attractiveness with respect to alternatives. Such considerations are part of the strategic assessment that concur in the determination of the treatment plan for the individual case.

### R8.5 | Which are the specific considerations when incorporating dental implants in stage IV periodontitis patients?

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| PICOS question addressed by a SR  |
| R8.5 - Expert consensus-based recommendation  |
| <i>When dental implants are considered in the rehabilitation of stage IV periodontitis patients, we <b>recommend</b> that information on the increased risk for peri-implantitis and implant loss should be provided.</i> |
| <b>Supporting literature</b> Expert opinion, (Carra et al., 2021; Lindhe, Meyle, & Group, 2008)   |
| <b>Quality of evidence</b> Low  |
| <b>Grade of recommendation</b> Grade A - ↑↑   |
| <b>Strength of consensus</b> Consensus (23.8% of the group abstained due to potential Col)  |

### Background

Substantial evidence indicates that subjects with advanced/rapidly progressing forms of periodontitis have a higher risk of implant loss and peri-implantitis compared to the general population (Carra et al., 2021; Schwarz, Derks, Monje, & Wang, 2018). While some of the risk seems to be associated with placement of dental implants before achievement of full control of periodontitis and, perhaps, with subjects with nicotine addiction who cannot quit cigarette smoking, the available evidence does not allow excluding that a portion of the increased risk

associated with periodontitis may persist even after appropriate periodontal treatment. The assumption that the health and function of dental implants in adequately treated and well-maintained stage IV periodontitis patients parallels the longevity observed for dental implants in the general population is probably optimistic.

In the systematic review by Carra et al. (2021), based on 7 prospective and 10 retrospective studies, accounting for 1,718 implants placed in patients with a history of periodontitis and 2,879 implants placed in patients with no history of periodontitis to restore multiple, eight out of 17 studies (47%) included both non-smokers and smokers, the latter group representing 1.7%-28.8% of the patient sample; one study considered non-smokers only, and the remaining seven studies did not provide any detail about smoking habits. The type of supportive periodontal/implant care was reported in only 11/17 studies (64.7%) but the patient's compliance to the recall intervals was rarely defined. Although the overall mean implant survival rate, at a follow-up of at least 5 years, was high also in patients with a history of periodontitis (94.7%, 95% CI [92.3%-97.1%]), pooled data analysis demonstrates that implant-supported fixed dental prostheses have a greater risk of failure (risk ratio - RR: 1.9, 95% CI [1.31-2.79]) and peri-implantitis (RR: 3.3, 95% CI [1.31-8.3]) in patients with a history of periodontitis, compared with patients with no history of periodontitis. The magnitude of the risk was considered clinically relevant, particularly after 5 years of follow-up from implant loading (hazard ratio - HR: 2.11, 95% CI [1.18-3.79]).

#### R8.6 | Which are the specific considerations for the design of dental implants restorations in stage IV periodontitis patients?

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| PICOS question addressed by a SR   |
| R8.6 - Expert consensus-based recommendation   |
| <i>Due to the risk of tooth loss and prosthesis failure, we <b>suggest</b> avoiding combined tooth/implant-supported fixed partial dental prostheses if alternatives are feasible.</i> |
| <b>Supporting literature</b> Expert opinion, (Montero et al., 2021)  |
| <b>Quality of evidence</b> Low   |
| <b>Grade of recommendation</b> Grade B - ↑   |
| <b>Strength of consensus</b> Unanimous Consensus (7.8% of the group abstained due to potential Col)  |

**Background**

Long-term studies have shown that dental prostheses retained by a combination of teeth and dental implants show higher rates of failure and tooth loss compared to dental prostheses supported by teeth or implants alone. In treatment planning, whenever alternatives exist, such designs should be avoided.

## 9 | CLINICAL RECOMMENDATIONS – CASE TYPE 3

### *Case type 3 - partially edentulous patients that can be prosthetically restored without full-arch rehabilitation*

#### 9.1 | Clinical recommendations for case type 3 with tooth-delimited gaps

**R9.1 | What is the effectiveness of prosthetic rehabilitation in patients with periodontitis stage IV where tooth preservation is feasible, with one or multiple tooth-delimited gaps, and adequate residual periodontal support and maintainability of the remaining teeth?**

*(Common question for Recommendations R9.1, R9.2, R9.3, R9.4)*

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| <b>PICOS question addressed by a SR</b>  |
| <b>R9.1 - Evidence-based recommendation</b>  |
| <i>In partially edentulous stage IV periodontitis patients with tooth-delimited edentulous spaces, different options (namely tooth-supported fixed dental prostheses, implant-supported fixed dental prostheses, removable dental prostheses, or no prosthetic rehabilitation) <b>may be considered.</b></i> |
| <b>Supporting literature</b> (Carra et al., 2021; Gotfredsen et al., 2021; Montero et al., 2021)   |
| <b>Quality of evidence</b> Low   |
| <b>Grade of recommendation</b> Grade O - ↔   |
| <b>Strength of consensus</b> Consensus (1.4% of the group abstained due to potential Col)  |

#### **Background**

##### Intervention

Interventions include tooth-supported fixed dental prostheses, implant-supported fixed dental prostheses, removable dental prostheses (RDPs), or no prosthetic rehabilitation, in periodontitis stage IV patients with one or multiple tooth-delimited gaps, and adequate residual periodontal support and maintainability of the remaining teeth.

##### Available evidence

###### *Number and design of included studies*

For **implant-supported fixed dental prostheses (iFDPs)** (Carra et al., 2021), evidence is based on 7 prospective and 10 retrospective studies, reporting on 1,718 implants placed in patients



with a history of periodontitis and 2,879 implants placed in patients with no history of periodontitis.

For **tooth-supported fixed dental prostheses (tFDPs)** (Montero et al., 2021), evidence is based on one RCT, one CCT, four prospective case series and 14 retrospective case series, including data from 1,029 subjects at baseline, with a total of 1,037 tFDPs, including 3,186 abutment teeth. The follow-up ranged between 24 and 425 months. At the end of the follow-up period, 933 subjects with 915 tFDPs on 2,989 abutment teeth were analysed.

For **removable dental prostheses (RDPs)** (Gotfredsen et al., 2021), evidence is based on three prospective (one RCT / two non-randomized) and one retrospective study, that specifically reported having also included Kennedy class III or IV RDPs (including minimum 175 to maximum 234, in total), and reporting on 1-5 years results, in either purely periodontitis patients or mixed populations. Several studies did not specify the type of Kennedy class.

#### *Risk of bias*

For **iFDPs**, 10/17 studies (58.8%) were considered at low risk of bias (Newcastle Ottawa Scale). Funding sources and conflict of interest declaration were not reported in the majority of studies.

For **tFDPs**, all investigations (n=20) presented an unclear or high risk of bias, using the RoB 2.0 tool, the ROBINS-I tool or the Newcastle-Ottawa Scale.

For **RDPs**, all four publications that specifically reported having also included Kennedy class III or IV RDPs, were judged being of moderate risk of bias (the RCT with the RoB 2.0 tool and the three non-randomized studies with the Newcastle Ottawa Scale). Funding sources and conflict of interest declaration were inconsistently reported.

#### *Effect sizes and their clinical relevance*

For **iFDPs**, although the risk of peri-implantitis and implant loss is greater in patients with a history of periodontitis compared to with patients with no history of periodontitis, the overall mean implant survival rate at a follow-up of at least 5 years is favourable (94.7% [92.3%-97.1%]) and acceptable to counterbalance the risks.

For **tFDPs**, the incidence of abutment-teeth loss after a follow-up period from 2 to 35.4 years was low (n=17 studies; weighted mean incidence (WMI)=4.8%; 95% confidence interval (CI) [3.2, 6.5]). The corresponding figure for prosthesis failure was WMI=6.9% (n= 18 studies; 95%

CI [4.1, 9.7]). Therefore, tFDPs seemed to be a valid alternative to restore function in patients with stage IV periodontitis.

For **RDPs**, out of the four publications that specifically reported having also included Kennedy class III or IV RDPs, in one publication (a prospective cohort study), an abutment tooth failure rate (defined as abutment tooth restoration or loss) ranging from of 16% - 48% was reported; however, it was not possible to attribute specific rates to a particular Kennedy class or type of RDP. In the RCT, specifically reporting that also included Kennedy class III or IV RDPs, an abutment failure rate of 9-15% was reported. However, it was not possible to attribute specific rates to a particular Kennedy class; the risk for failure was higher at non-vital compared with vital abutment teeth (hazard ratio, HR=2.29).

### *Consistency*

For the **iFDPs**, sensitivity analysis indicated consistency.

For **tFDPs**, a significant publication bias was observed for the main outcome measure (i.e., tooth loss).

For **RDPs**, no analysis of the consistency was possible based on the available evidence.

### *Balance of benefit and harm*

Specific analyses on benefits/risks ratio comparing different options for the rehabilitation of unilateral or bilateral posterior free-end edentulism were not the focus of the systematic reviews.

For **iFDPs**, potential harms related to surgery (e.g., intra- and post-operative complications) and peri-implant health maintenance (e.g., higher risk of peri-implantitis and implant loss over time) should be considered.

For **tFDPs**, technical complications (e.g., loss of retention, framework fracture, porcelain fracture, etc.) presented a WMI=13.6% (n= 10 studies; 95% CI [8.3, 18.9]) and seemed to be more frequent than biologic complications (e.g., caries, endodontic failure, root fracture, etc.) that presented a WMI=5.1% (n=7 studies, 95% CI [2.5, 7.8]).

**RDPs** does not necessarily cause further periodontal breakdown or tooth loss, but there is also no information in the studies that specifically reported, having also included Kennedy class III or IV RDPs, on whether masticatory efficiency, including nutritional status, or OHRQoL were improved.

### Overall certainty of the evidence

For **iFDPs**, the certainty of evidence is moderate.

For **tFDPs**, the certainty of evidence is low.

For **RDPs**, the certainty of evidence is low.

### From evidence to recommendation- additional considerations

#### *Acceptability*

**iFDPs** are acceptable, and a widespread option for rehabilitation of partial edentulism in patients with stage IV periodontitis. Little is known about patients' preferences and satisfaction.

Patient satisfaction was considered in seven studies evaluating **tFDPs**, using questionnaires related to chewing function, aesthetics, phonetics, comfort and/or general satisfaction. In general, more than 85% of the patients were satisfied with the treatment provided or reported positive results for the different outcomes evaluated.

**RDPs** are acceptable and a widespread option for rehabilitation of partial edentulism in patients with stage IV periodontitis. Little is known about patients' preferences and satisfaction.

#### *Feasibility*

**iFDPs** are demanding in terms of professional competency and resources.

**tFDPs** are demanding in terms of professional competency and resources.

**RDPs** are often less demanded comparing to tFDPs or iFDPs.

#### *Ethical Considerations*

Not applicable.

#### *Economic Considerations*

**iFDPs** imply additional costs that are not covered by healthcare systems in most countries and may be source of inequality.

The economic considerations related with **tFDPs** have not been properly evaluated. In any case, they may imply additional costs that are not covered by healthcare systems in most countries and may be source of inequality.

**RDPs** are more economical comparing to tFDPs or iFDPs and often covered (at least partially) by most healthcare systems.

*Legal Considerations*

Not applicable.

**R9.2 | See question for R9.1**

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| PICOS question addressed by a SR   |
| R9.2 - Evidence-based recommendation   |
| <i>We <b>suggest</b> using tooth-supported fixed dental prostheses in patients with stage IV periodontitis when abutment teeth are periodontally maintainable and restorable. Resin-bonded fixed dental prostheses <b>may be considered</b> in certain circumstances (e.g. small tooth delimited edentulous spaces).</i> |
| <i>We <b>suggest not to use</b> resin-bonded fixed dental prostheses for large tooth-delimited edentulous spaces.</i>  |
| <b>Supporting literature</b> (Montero et al., 2021)  |
| <b>Quality of evidence</b> Low   |
| <b>Grade of recommendation</b> Grade B – ↑ / Grade O - ↔ / Grade B - ↑   |
| <b>Strength of consensus</b> Consensus (4.9% of the group abstained due to potential Col)  |

**Background**

Intervention

For tooth-supported fixed dental prostheses (tFDPs), see the background text of Recommendation R9.1.

In certain cases, for example in small, tooth-delimited edentulous spaces, minimally- or non-invasive resin-bonded fixed dental prostheses (FDPs) can be alternatively considered.

Available evidence

*Number and design of included studies*

Two case series (one prospective and one retrospective) evaluating 80 patients and 99 resin-bonded FDPs in mandibular anterior teeth.

#### *Risk of bias*

Both studies presented a high risk of bias according to the Newcastle-Ottawa scale.

#### *Effect sizes and their clinical relevance*

No tooth loss was reported but a high incidence of prostheses failure (WMI= 27.4%, 95% CI [-6.7, 61.4]) was observed. Therefore, this treatment option may be considered only in specific clinical scenarios (e.g., missing single anterior teeth).

#### *Consistency*

No analysis of the consistency was possible based on the available evidence.

#### *Balance of benefit and harm*

Even if prosthetic complications may be expected in resin-bonded FDPs, most of the cases were solved with minor reparations. Moreover, it must be highlighted that teeth used as abutment were minimally prepared.

#### *Overall certainty of the evidence*

Low.

#### *From evidence to recommendation- additional considerations*

##### *Acceptability*

General satisfaction and aesthetics were evaluated in both studies with high rates for both outcomes (over 8.5/10 in visual analogue scales).

##### *Feasibility*

Resin-bonded FDPs are demanding in terms of professional competency and resources.

##### *Ethical Considerations*

Not applicable.

### *Economic Considerations*

Resin-bonded FDPs may be a more affordable alternative to other tooth-supported FDPs.

### *Legal Considerations*

Not applicable.

### **R9.3 | See question for R9.1**

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| PICOS question addressed by a SR  |
| R9.3 – Evidence-based recommendation  |
| <i>We <b>suggest</b> using implant-supported fixed dental prostheses when abutment teeth are not periodontally maintainable and restorable.</i> |
| <b>Supporting literature</b> (Carra et al., 2021)   |
| <b>Quality of evidence</b> Low  |
| <b>Grade of recommendation</b> Grade B – ↑ / Statement  |
| <b>Strength of consensus</b> Strong consensus (2.1% of the group abstained due to potential Col)  |

### **Background**

#### Intervention

Rehabilitation with implant-supported fixed dental prostheses, in periodontitis stage IV partially edentulous patients, with one or multiple tooth-delimited gaps, and abutment teeth that are not periodontally maintainable and restorable.

For further detail, see the sections dealing with implant-supported fixed dental prostheses in the background text for Recommendation R9.1.

### **R9.4 | See question for R9.1**

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| PICOS question addressed by a SR  |
| R9.4 - Evidence-based recommendation  |
| <i>Metal-based frame removable dental prostheses <b>may be considered</b> as transitional or definitive treatment options when a fixed solution is not a consideration.</i> |
| <b>Supporting literature</b> (Gotfredsen et al., 2021)  |
| <b>Quality of evidence</b> Low  |

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| <b>Grade of recommendation</b> Grade O - ↔  |
| <b>Strength of consensus</b> Consensus (0% of the group abstained due to potential Col) |

## **Background**

### Intervention

Patients diagnosed of stage IV periodontitis and missing teeth frequently require an interim removable dental prosthesis (RDP) to ensure chewing function by increasing the number of occlusal units (antagonistic pairs in premolar and molar region) and/or to replace anterior teeth for esthetic reasons.

Steps 1 and 2 of periodontal therapy are accompanied by a reduction in inflammation and swelling, which becomes frequently visible as gingival recession, while tooth extractions lead to remodeling of the alveolar bone associated with morphological tissue changes. In the light of this background, any interim RDP has to be designed with an occlusal rest on the residual dentition in order to avoid any trauma to periodontal tissues and teeth from a sinking prosthesis. Before taking the initial impression or intraoral scan, the intermaxillary situation is evaluated and teeth with a good prognosis are considered as abutment teeth. Depending on the occlusal situation and the available space, abutment teeth should be provided with a shallow occlusal rest preparation. On the resulting situation model, which is used to fabricate the interim RDP, teeth to be extracted are removed in plaster, and clasps are manually bent. These clasps with occlusal rests ensure sufficient stability during the phase of tissue remodeling, after which relining of the prosthesis basis or fabrication of a definitive RDP is frequently indicated.

After successful periodontal therapy and when post-extraction tissue changes have occurred, the interim prosthesis can be replaced by a definitive removable dental prosthesis. For retention of the RDP, 2-4 abutment teeth with good prognosis and a wide spread (distributed anterior and posterior) are used. The retention element is selected depending on the condition of the coronal tooth substance, esthetic demands and financial conditions:

- An intact, caries-free tooth is best provided with a clasp or an adhesive attachment (Zitzmann, Rohner, Weiger, & Krastl, 2009). While a clasp abutment tooth can have fillings of small extent, a tooth intended for an adhesive element with an extracoronal attachment should have sound enamel surfaces to ensure adhesive cementation. These resin-bonded attachments for precision-retained RPD are compatible with periodontal health, ensure occlusal rests, require minimal tooth preparation and provide very good aesthetics results. To ensure periodontal health, clasps are designed with vertical support by an occlusal rest (ideally located on sound tooth structure), and a stiff reciprocal part neutralizing lateral forces during prosthesis insertion and removal.
- Decayed teeth and those with extended fillings are better restored with telescopes or crowns with clasps (Zitzmann et al., 2009).
- For abutment teeth with a destroyed clinical crown, root canal treatment is frequently required and the root cap provided with a post and a retentive element is the most appropriate solution to retain the overdenture prosthesis.

For further detail, see the sections dealing with removable dental prostheses in the background text for Recommendation R9.1.

## 9.2 | Clinical recommendations for case type 3 with unilateral or bilateral posterior free-end edentulism

**R9.5 | In patients with a periodontally compromised dentition due to stage IV periodontitis or equivalent, what is the efficacy of various prosthetic restorative options for the rehabilitation of unilateral or bilateral posterior free-end edentulism?**

*(Common question for Recommendations R9.5, R9.6, R9.7)*

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| PICOS question addressed by a SR   |
| R9.5 - Evidence-based recommendation   |
| <i>For the rehabilitation of partially edentulous stage IV periodontitis patients with free end situations different options (namely shortened dental arch, implant-supported restorations or removable dental prostheses) <b>may be considered.</b></i> |
| <b>Supporting literature</b> (Carra et al., 2021; Gotfredsen et al., 2021; Montero et al., 2021)   |
| <b>Quality of evidence</b> Low   |



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| <b>Grade of recommendation</b> Grade O - ↔   |
| <b>Strength of consensus</b> Strong consensus (0% of the group abstained due to potential Col) |

## Background

### Intervention

Interventions include shortened dental arch, implant-supported fixed dental prostheses (iFDPs) or removable dental prostheses (RDPs), in periodontitis stage IV patients with unilateral or bilateral posterior free-end edentulism. See also the background text of Recommendation R9.1.

### Available evidence

#### *Number and design of included studies*

For **iFDPs**, evidence is based on 7 prospective and 10 retrospective studies, including accounting for 1,718 implants placed in patients with a history of periodontitis and 2,879 implants placed in patients with no history of periodontitis.

For the **shortened dental arch**, the evidence is based on seven RCTs and five non-randomized studies (four prospective and one retrospective), including from 10 to 79 patients per group at final examination, either having shortened dental arch or restored to shortened dental arch; however, most of the publications included <50 patients/RPDs per group. Publications report mostly on 1-year data (one study presents 10-year results), in either purely periodontitis patients or mixed populations.

For **RDPs**, evidence is based on 12 RCTs including from 19 to 79 patients/RDP per group at the final evaluation, six prospective cohort studies including from 10 to 703 patients/RDP per group at the final evaluation, and three retrospective studies, including from 15 to 25 patients/RPD per treatment group; however, most of the publications included <50 patients/RPD per group. Most studies reported on Kennedy class I & II. The studies reported on 1 to 10-year results, with several reporting on 5-year data, in either purely periodontitis patients or mixed populations.

### *Risk of bias*

For **iFDPs**, 10/17 studies (58.8%) were considered at low risk of bias (Newcastle Ottawa Scale). Funding sources and conflict of interest declaration were not reported in the majority of studies.

For the **shortened dental arch**, five out of seven RCTs present some concerns regarding risk of bias (RoB 2.0 tool), while among the five non-randomized studies, one was judged of high risk, four were judged of moderate risk, and only one was judged of low risk (Newcastle Ottawa Scale).

For **RDPs**, in 10 out of 12 RCTs, some concerns regarding risk of bias (RoB 2.0 tool) were found, while in the nine non-randomized studies, two were judged of high risk, six were judged of moderate risk, and only one was judged of low risk (Newcastle Ottawa Scale). Funding sources and conflict of interest declaration were inconsistently reported

#### *Effect sizes and their clinical relevance*

For **iFDPs**, although the risk of peri-implantitis and implant loss is greater in patients with a history of periodontitis, compared to with patients with no history of periodontitis, the overall mean implant survival rate at a follow-up of at least 5 years is favourable (94.7%, 95% CI [92.3%-97.1%]) and acceptable to counterbalance the risks.

For the **shortened dental arch**, two studies show a lower risk for tooth loss compared with patients with an RDP (odds ratio - OR=1.92; hazard ratio - HR=1.24), but it was not consistently significant. In a few studies, the shortened dental arch is associated with significantly lower plaque values and/or gingival inflammation compared with RDPs, and less gingival recession, comparing to abutment teeth of RDPs. A shortened dental arch does not necessarily imply lower masticatory efficiency, including nutritional status, or worse OHRQoL compared with patients with RDPs.

For **RDPs**, abutment tooth failure rates of 9%-48% have been reported in two studies comparing different types of RDPs, but these were not possible to attribute to specific Kennedy class and the differences were not significant. Two studies show a higher risk for tooth loss in patients with an RDP compared to no treatment (OR=1.92; HZ=1.24), but it was not consistently significant. In a few studies, RDPs are associated with significantly more plaque values and/or gingival inflammation, and more recession at abutment teeth with clasps, but not necessarily with more significant other periodontal problems. RDPs do not

necessarily increase masticatory efficiency, including nutritional status, or improve OHRQoL compared with a short dental arch.

### *Consistency*

For **iFDPs**, sensitivity analysis indicated consistency.

For the **shortened dental arch**, no analysis was possible.

For **RDPs**, no analysis was possible.

### *Balance of benefit and harm*

Specific analyses on benefits/risks ratio comparing different options for the rehabilitation of unilateral or bilateral posterior free-end edentulism were not the focus of the systematic reviews.

For **iFDPs**, potential harms related to surgery (e.g., intra- and post-operative complications) and peri-implant health maintenance (e.g., higher risk of peri-implantitis and implant loss over time) should be considered.

Preserving- or restoring to a **shortened dental arch**, does not necessarily cause further periodontal breakdown or tooth loss, but is also not necessarily associated with reduced masticatory efficiency or nutritional status, or reduced OHRQoL.

**RDPs** do not necessarily cause further periodontal breakdown or tooth loss but are also not necessarily associated with increased masticatory efficiency, including nutritional status, or improve OHRQoL.

### *Overall certainty of the evidence*

For **iFDP**, the certainty of evidence is moderate.

For the **shortened dental arch**, the certainty of evidence is low.

For **RDPs**, the certainty of evidence is low.

### *From evidence to recommendation- additional considerations*

#### *Acceptability*

**iFDPs** are acceptable, and a widespread option for rehabilitation of partial edentulism in patients with periodontitis. Little is known about patients' preferences and satisfaction.

No restorative treatment or restoring to a **shortened dental arch** intervention is an acceptable treatment option associated with little risks. Little is known about patients' preferences and satisfaction.

**RDPs** are acceptable and a widespread option for rehabilitation of partial edentulism in patients with periodontitis. Little is known about patients' preferences and satisfaction.

#### *Feasibility*

**iFDPs** are demanding in terms of professional competency and resources.

Restoring to a **shortened dental arch** may not be a very demanding treatment option.

**RDPs** are less demanding comparing to tooth- or implant supported fixed dental prostheses.

#### *Ethical Considerations*

Not applicable.

#### *Economic Considerations*

**iFDPs** imply additional costs that are not covered by healthcare systems in most countries and may be source of inequality.

No restorative treatment or restoring to a **shortened dental arch** may be the most economical solution.

**RDPs** are more economical comparing to tooth- or implant supported fixed dental prostheses and often covered (at least partially) from most healthcare systems.

#### *Legal Considerations*

Not applicable.

### **R9.6 | See question for R9.5**

PICOS question addressed by a SR

R9.6 - Evidence-based recommendation

*In stage IV periodontitis patients with a shortened dental arch with sufficient occluding/masticatory units (e.g., from second premolar to second premolar, no evident risk for flaring or tooth elongation and adequate patient comfort) no tooth replacement **may be considered** in the free-end situation.*

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| <b>Supporting literature</b> (Gotfredsen et al., 2021; Kayser, 1981; Walter et al., 2018; Walter et al., 2020) |
| <b>Quality of evidence</b> Low   |
| <b>Grade of recommendation</b> Grade O - ↔   |
| <b>Strength of consensus</b> Simple majority (0% of the group abstained due to potential Col)                  |

## Background

### Intervention

No restorative treatment in situations with sufficient occluding/masticatory units. See the background text for Recommendation R9.5.

## R9.7 | See question for R9.5

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| PICOS question addressed by a SR   |
| R9.7 - Evidence-based recommendation   |
| <i>In stage IV periodontitis patients with free-end situations who require additional occluding units, we <b>suggest</b> implant-supported fixed dental prostheses.<br/>When implants are not an option, we <b>suggest</b> removable dental prostheses with a metal-based framework.</i> |
| <b>Supporting literature</b> (Carra et al., 2021; Gotfredsen et al., 2021)   |
| <b>Quality of evidence</b> Low   |
| <b>Grade of recommendation</b> Grade B - ↑ / Grade B - ↑   |
| <b>Strength of consensus</b> Strong consensus (1.9% of the group abstained due to potential Col)   |

## Background

### Intervention

Interventions include implant-supported fixed dental prostheses or removable dental prostheses with a metal-based framework, to restore free-end partial edentulism in periodontitis stage IV patients. See the background text of Recommendation R9.1 for information on implant-supported fixed dental prostheses, and the background text of Recommendation R9.5 for information on removable dental prostheses, respectively.

## 10 | CLINICAL RECOMMENDATIONS – CASE TYPE 4

*Case type 4 - partially edentulous patients that need to be restored with full-arch rehabilitation, either tooth- or implant-retained*

**R10.1 | In patients with a compromised dentition due to stage IV periodontitis with a sufficient number of adequately distributed teeth, what is the performance of tooth-supported full-arch fixed prostheses?**

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| PICOS question addressed by a SR  |
| R10.1 - Evidence-based recommendation   |
| <i>In patients with periodontitis stage IV with a sufficient number (<math>\geq 4</math> abutment teeth) of periodontally maintainable, bilaterally distributed and restorable teeth in the maxilla and/or mandible, we <b>suggest</b> a tooth-supported full-arch fixed dental prosthesis.</i> |
| <b>Supporting literature</b> (Montero et al., 2021; Tomasi et al., 2021)  |
| <b>Quality of evidence</b> Low  |
| <b>Grade of recommendation</b> Grade B – ↑  |
| <b>Strength of consensus</b> Consensus (1.6% of the group abstained due to potential Col)   |

### Background

#### Intervention

Tooth-supported full-arch fixed prostheses were used to restore function and aesthetics. The treatment strategy commonly included the use of a fixed interim restoration during the early steps of periodontal therapy.

#### Available evidence

##### *Number and design of included studies*

Seven studies (n=522 patients) with a weighted mean follow-up period of 8.6 years were included. All studies were of observational and retrospective design and outcome measures included tooth loss, loss of restoration and occurrence of technical complications. Biological complications, PROMs, health economic parameters and adverse events were not consistently reported.

##### *Risk of bias*

All included studies were judged to present with a high risk of bias, mainly due to confounding and outcome assessment.

#### *Effect sizes and their clinical relevance*

Based on three studies (n=165 patients), tooth loss over a period of 12.7 years was estimated at 4.9% (95% CI 2%-14%). Based on four studies (n=415 patients), loss of restoration over an observation period of 9.7 years was estimated at 4.6% (95% CI 2%-14%). During an observation period of 7.2 years in three studies (n=365 patients), the overall occurrence of technical complications at the restoration level was 8.0% (95% CI 6%-11%).

#### *Consistency*

Results were consistent across studies. The evidence considered has been generated by a small group of investigators and external applicability is unclear.

#### *Balance of benefit and harm*

High survival rates and low incidence of complications were observed. PROMs were not considered in the available studies. A tooth-supported fixed restoration may not address some functional and/or aesthetic needs in specific patients (e.g. when in need for facial tissue and lip support, or in cases of soft tissue deficiencies or long abutment teeth).

#### *Overall certainty of the evidence*

The certainty of evidence is graded as low based on the observational, retrospective design of studies and the high risk of bias.

#### *From evidence to recommendation- additional considerations*

##### *Acceptability*

PROMs were not reported in the identified studies (Tomasi et al., 2021). Data summarized by Montero et al. (Montero et al., 2021) on tooth-supported fixed partial and full-arch prostheses suggest a high rate of patient satisfaction.

##### *Feasibility*

Related procedures are clinically and technically demanding.

*Ethical Considerations*

Not applicable.

*Economic Considerations*

Health-economic parameters were not evaluated in the identified studies. Different restorative materials and technical approaches may increase affordability. Due to complexity of execution and cost of this alternative, some patients may elect to proceed with palliative care consisting of a transitional denture retained by few residual teeth or a full denture.

*Legal Considerations*

Not applicable.

**R10.2 | In patients with a compromised dentition due to stage IV periodontitis, what is the performance of tooth-supported full-arch removable prostheses?**

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| PICOS question addressed by a SR   |
| R10.2 - Evidence-based recommendation (voted as R3.B-1)  |
| <i>In periodontitis stage IV patients with an insufficient number/distribution of periodontally maintainable teeth to support a tooth-supported full-arch fixed dental prosthesis, a tooth-supported full-arch removable dental prosthesis (overdenture) <b>may be considered.</b></i> |
| <b>Supporting literature</b> (Donos et al., 2021)  |
| <b>Quality of evidence</b> Very low  |
| <b>Grade of recommendation</b> Grade O - ↔   |
| <b>Strength of consensus</b> Strong consensus (0% of the group abstained due to potential Col)   |

**Background**

*Intervention*

In patients with an insufficient number and/or distribution of periodontally maintainable teeth to support a full-arch fixed prosthesis in the maxilla/mandible, clinicians may consider a tooth-supported removable full-arch prosthesis (TSRP). TSRP can be realized through different retention/attachment systems (e.g. ball-cap, magnetic) and the abutment teeth may or may not be splinted.



### Available evidence

#### *Number and design of included studies*

Twenty-two studies (10 prospective and 12 retrospective studies) were included reporting on 4,579 abutment teeth and 1,660 TSRPs. The prospective studies had a weighted mean follow-up of 36.9 months for tooth survival and 86.5 months for prosthesis survival, while the retrospective studies had a weighted mean follow-up of 83.3 months for tooth survival and 75.2 months for prosthesis survival. Outcome measures included tooth loss and loss of restoration. Occurrence of technical and biological complications as well as PROMs and health economic parameters and adverse events were not consistently reported.

#### *Risk of bias*

All included studies were judged to present with a high risk of bias.

#### *Effect sizes and their clinical relevance*

The prospective studies suggested a tooth survival rate (tooth level) ranging from 86% to 100% over a weighted mean follow-up of 36.9 months. The retrospective studies showed a range of survival from 34% to 94% at tooth level (weighted mean follow-up 83.3 months) and from 38% to 100% at prosthesis level (weighted mean level 75.2 months).

#### *Consistency*

Treatment strategies varied across studies and sensitivity analyses were not feasible. The evidence considered has been generated by a small group of investigators and external validity is unclear.

#### *Balance of benefit and harm*

The evidence suggests heterogenous outcomes in terms of prosthesis and tooth survival. The lack of information on complications should be considered.

### Overall certainty of the evidence

The certainty of evidence is graded as very low based on study design, heterogenous outcomes and high risk of bias.

### *From evidence to recommendation- additional considerations*

#### *Acceptability*

PROMs were reported in 9 of the included studies. The tools used to assess PROMs were not validated and inconsistent across studies.

#### *Feasibility*

Related procedures are clinically and technically demanding.

#### *Ethical Considerations*

The preservation of abutment teeth might offer a psychological benefit for patients who are transitioning to edentulism.

#### *Economic Considerations*

Health-economic parameters were not evaluated in the identified studies. TSRPs entail costs related to periodontal and prosthetic treatment.

#### *Legal Considerations*

Not applicable.

**R10.3 | In patients with a compromised dentition due to stage IV periodontitis in whom tooth preservation was deemed impossible, what is the performance of implant-supported full-arch fixed prostheses?**

|   |
|---|
| PICOS question addressed by a SR  |
| R10.3 - Evidence-based recommendation   |
| <i>In periodontitis stage IV patients in whom tooth preservation was deemed impossible, and a sufficient number (<math>\geq 4</math>) of bilaterally distributed and adequately sized dental implants are planned in the maxilla and/or mandible, we <b>suggest</b> an implant-supported full-arch fixed dental prosthesis.</i> |
| <b>Supporting literature</b> (Ramanauskaite et al., 2021; Tomasi et al., 2021)  |
| <b>Quality of evidence</b> Low  |
| <b>Grade of recommendation</b> Grade B - $\uparrow$   |
| <b>Strength of consensus</b> Consensus (33.3% of the group abstained due to potential Col)  |

**Background**

Intervention

Implant-supported full-arch fixed prostheses were used to restore function and aesthetics on  $\geq 4$  implants in the same jaw. Prosthetic restorations were predominantly screw-retained and installation protocols, i.e. immediate vs. delayed implant installation, varied across studies.

Available evidence

*Number and design of included studies*

19 studies (n=1,189 patients) with a weighted mean follow-up period of 3.6 years were included. The majority of studies were observational and designed as prospective case series. Consistently reported outcome measures included loss of implants, loss of restorations and occurrence of technical and biological complications. Data on PROMs and health economic parameters were not consistently reported.

*Risk of bias*

All included studies were judged to present with a high risk of bias, mainly due to confounding and outcome assessment.

*Effect sizes and their clinical relevance*

Based on 15 studies (n=670 patients), implant loss over an observation period of 3.9 years was estimated at 3.5% (95% CI 2%-7%). Loss of restorations, as reported in nine studies (n=766 patients), was estimated to be 4.6% (95% CI 1%-18%) during an observation period of 3.2 years. Over a follow-up period of 2.6 years (9 studies, 723 patients), technical complications affected 41.7% (95% CI 25%-68%) of all restorations. Biological complications were evaluated in 12 studies (n=984 patients), covering a time period of 3.1 years and 8.5% (95% CI 5%-13%) of all implants developed at least one biological complication.

### *Consistency*

Results were consistent across studies. The evidence considered has been generated by a small group of investigators and external applicability is unclear.

### *Balance of benefit and harm*

High survival rates of restorations and implants were observed. The high rate of technical complications over short observation periods should be considered, as should be the limited information on PROMs. An implant-supported fixed restoration may not address some functional and/or aesthetic needs in specific patients (e.g. when in need for facial tissue and lip support, or in cases of soft tissue deficiencies).

### *Overall certainty of the evidence*

The certainty of evidence is graded as low based on study design and limited follow-up periods.

### *From evidence to recommendation- additional considerations*

#### *Acceptability*

PROMs were reported in two studies (n=22 patients) indicating a high level of patient satisfaction.

#### *Feasibility*

Related procedures are demanding in terms of professional competence and resources.

#### *Ethical Considerations*

Not applicable.

#### *Economic Considerations*

Health-economic parameters were evaluated in one (n=56 patients) of the identified studies.

#### *Legal Considerations*

Not applicable.

**R10.4 | In patients with a compromised dentition due to stage IV periodontitis in whom tooth preservation was deemed impossible, what is the performance of implant-supported full-arch removable prostheses?**

|  |
|--|
| PICOS question addressed by a SR   |
| R10.4 - Evidence-based recommendation  |
| <i>In periodontitis stage IV patients in whom tooth preservation was deemed impossible and adequately sized dental implants can be used, albeit not in sufficient number and/or adequate position to support a full-arch fixed dental prosthesis, an implant-supported full-arch removable dental prosthesis (overdenture) <b>may be considered.</b></i> |
| <b>Supporting literature</b> (Donos et al., 2021; Ramanauskaite et al., 2021)  |
| <b>Quality of evidence</b> Very low  |
| <b>Grade of recommendation</b> Grade O - ↔   |
| <b>Strength of consensus</b> Strong consensus (37.0% of the group abstained due to potential Col)  |

#### **Background**

##### Intervention

In edentulous patients in whom the insertion of a sufficient number ( $\geq 4$ ) of bilaterally distributed and adequately sized dental implants is not feasible, clinicians may consider an implant-supported removable prosthesis (ISRP). ISRPs can be supported/retained by a number of different attachment systems. The most commonly used systems include stud, bar, magnetic and telescopic attachments. Implants may or may not be splinted.

##### Available evidence

### *Number and design of included studies*

Five studies (n=136 patients) with a weighted mean follow-up period of 3.3 years were included. Four studies were of prospective and one of retrospective design. All studies were observational and used conventional loading protocols. The consistently reported outcome measures included survival of ISRPs and implants. Data on technical and biological complications, PROMs and health economic parameters were not (consistently) reported.

### *Risk of bias*

All studies had a high or critical risk of bias, thus raising concerns on the possibility of drawing robust conclusions.

### *Effect sizes and their clinical relevance*

Prosthesis survival during the weighted mean follow-up period of 3.3 years was 100% and implant survival ranged from 96% to 100%.

### *Consistency*

Due to the limited number of studies, sensitivity analyses were not feasible. Treatment strategies varied considerably across studies.

### *Balance of benefit and harm*

The evidence suggests favourable outcomes in terms of prostheses and implant survival. The lack of information on complications and PROMs as well as the short follow-up should be considered.

### *Overall certainty of the evidence*

The certainty of evidence is graded as very low based on study design and high risk of bias.

### *From evidence to recommendation- additional considerations*

#### *Acceptability*

PROMs were reported in two of the included studies. The tools used to assess PROMs were not validated and inconsistent across studies.

*Feasibility*

ISRP-related procedures are clinically and technically demanding.

*Ethical Considerations*

Not applicable.

*Economic Considerations*

Health-economic parameters were not evaluated in the identified studies. ISRPs entail costs related to surgical and prosthetic treatment.

*Legal Considerations*

Not applicable.

## 11 | LONG-TERM OUTCOMES OF TREATMENT IN STAGE IV PERIODONTITIS PATIENTS

### 11.1 | Intervention - Professionally administered Supportive Periodontal Care (SPC)

The systematic review (Leow et al., 2021) assessed the role of professionally administered SPC in preventing tooth loss (TL), periodontitis progression (clinical attachment loss, CAL) and associated health outcomes in patients with periodontitis who had completed active periodontal treatment.

The role of SPC is highly relevant to patients with all stages of periodontitis. In the systematic review (Leow et al., 2021), it was not possible to identify studies focussed on stage IV periodontitis and the findings are therefore relevant to all stages of disease.

Five components or combinations thereof contribute to SPC interventions:

- 1) **Interview:** periodontal health symptoms, medical and social history, risk factors including tobacco use, stress, diabetes and reported plaque control regime;
- 2) **Assessment:** plaque and calculus deposits, periodontal health status, including inflammation, probing pocket depths and bleeding pockets;
- 3) **Evaluation:** intervention needs including risk factor management, oral hygiene and re-treatment;
- 4) **Practical Intervention:** oral hygiene coaching, instrumentation of supra- and sub-gingival plaque and calculus, treatment of sites with recurrence (finding of periodontitis at a previously healthy/stable site) or residual periodontitis (a deep periodontal pocket remains despite active therapy);
- 5) **Planning:** interval before next SPC visit. The control was no or irregular SPC, defined as greater than a frequency of 3-monthly.

Specialist and non-specialist settings were considered, and protocols included adjunctive therapies.

The primary outcome was tooth loss. Secondary outcomes included one site with CAL loss  $\geq$  2 mm, number of sites with probing pocket depths (PPD)  $\geq$  5 mm with bleeding on probing



(BoP); number of sites requiring re-treatment; Oral Health Related Quality of Life (OHRQoL) questionnaires; care cost analysis; other patient reported outcomes.

Studies of 5-10 years follow-up (n=17), over 10-years (n=7) and 20 years (n=2) were included. Nine studies addressed 12-month follow-up of treatment of recurrence, but high heterogeneity prevented conclusions on different treatment methods.

## 11.2 | Is regular, professionally administered, SPC effective in preventing tooth loss or disease recurrence in the longer term?

### R11.1 | Does regular SPC reduce tooth loss?

|   |
|---|
| PICOS question addressed by a SR  |
| R11.1 - Evidence-based recommendation (1), Expert consensus-based recommendation (2)  |
| <ol style="list-style-type: none"> <li><b>We recommend</b> provision of and adherence to regular professionally administered supportive periodontal care (SPC) to reduce tooth loss in the long term (<math>\geq 5</math> years).</li> <li><b>We recommend</b> that SPC should initially be provided at 3-monthly intervals. Medium to long-term frequency should be personalised to each individual patient, taking into account clinical and behavioral circumstances.</li> </ol> |
| <b>Supporting literature</b> (Leow et al., 2021)  |
| <p><b>Quality of evidence</b> Moderate</p> <p>For tooth loss: Seventeen prospective cohorts judged as 'low' risk of bias except one study with a 'moderate' risk using the Newcastle-Ottawa scale.</p> <p>For CAL loss <math>\geq 2</math> mm: Seven prospective cohorts whereby all were judged as 'low' risk of bias.</p>   |
| <b>Grade of recommendation</b> Grade A – ↑↑   |
| <b>Strength of consensus</b> Consensus (0% of the group abstained due to potential CoI)   |

## Background

### Intervention

Supportive periodontal care (SPC) includes preventative and/or therapeutic interventions for periodontitis patients who have been successfully treated for periodontitis. The goals of SPC are to maintain periodontal stability, by preventing disease recurrence or progression

and ultimately to prevent tooth loss. Adherence to professionally administered SPC at regular time intervals allows ongoing monitoring of periodontal status, practical interventions (as required) and formulation of individually tailored SPC time intervals based on patient risk.

### Available evidence

#### *Number and design of included studies*

Twenty-four prospective cohort studies. The primary outcome of the systematic review (Leow et al., 2021) was tooth loss. The secondary outcome, to inform on disease recurrence/progression was clinical attachment level (CAL) loss  $\geq 2$  mm.

Tooth loss: seventeen studies reported tooth loss and eight of these studies were included in the meta-analysis, contributing to tooth loss at a patient level (192 participants). The remaining nine studies were reported qualitatively.

Clinical attachment level loss  $\geq 2$  mm: seven studies reported on CAL loss  $\geq 2$  mm. Three studies contributed data to the meta-analysis for estimating the number of patients experiencing CAL loss  $\geq 2$  mm (86 participants), whilst the remaining four studies were reported qualitatively.

#### *Risk of bias*

Study quality assessment using the Newcastle-Ottawa scale, identified low risk of bias for all but two studies, which had a moderate risk of bias.

#### *Effect sizes and their clinical relevance*

“Regular” SPC was defined as 3-monthly, whilst a lack of adherence to or no SPC was described as “irregular”

Tooth loss: the mean proportion of patients who experienced tooth loss was 9.6% (95% CI 5%-14%) with low heterogeneity  $I^2=28\%$  ( $p=0.161$ ). 8% (95% CI 2%-14%) of regular attendees experienced tooth loss compared to 11.9% (95% CI 5%-19%) of irregular attendees. The difference between sub-groups was, however not statistically significant ( $p=0.161$ ). A greater length of follow-up ( $\geq 10$  years) associated with an increased experience of tooth loss of 12.7% (95% CI 4%-22%) compared with 8.2% (95% CI 3%-13%) for 5-10 years follow-up.

Clinical attachment level loss  $\geq 2$  mm: the mean proportion of patients who experienced overall CAL loss  $\geq 2$  mm was 24.8% (95% CI 11%-38%) with substantial heterogeneity  $I^2=63\%$  ( $p=0.013$ ). 30.2% (95% CI -2%-63%) of patients who attended regular SPC appointments experienced CAL loss  $\geq 2$  mm, compared to 21.4% (95% CI 10%-33%) of those who attended irregularly. The difference between subgroups was not statistically significant ( $p=0.332$ ). The unexpected result indicating that regular SPC may lead to a greater experience of CAL loss  $\geq 2$  mm is imprecise (large confidence interval). A greater length of follow-up ( $\geq 10$  years) was associated with a slight increase in CAL loss  $\geq 2$  mm of 26.3% (95% CI 8%-45%) compared with 22.1% (95% CI 5%-39%) for 5-10 years follow-up.

### *Consistency*

Heterogeneity across studies was identified for both tooth loss [ $I^2=28\%$  ( $p=0.161$ )] and CAL loss  $\geq 2$  mm [ $I^2=63\%$  ( $p=0.013$ )]. This may be explained by the limited number of studies fulfilling the inclusion criteria of the systematic review and/or the type of therapy carried out in the active periodontal treatment phase (regenerative or non-regenerative). Studies differed in terms of the different elements contributing to an SPC appointment and frequently did not report the operator(s) performing each visit.

### *Balance of benefit and harm*

Few studies reported adverse events. An overall consideration of the benefit versus harm of regular SPC supports the strength of the recommendation.

### Overall certainty of the evidence

Moderate.

### From evidence to recommendation- additional considerations

#### *Acceptability*

Little is known about patient preferences in relation to SPC. However, SPC has been recommended for oral healthcare for several decades.

#### *Feasibility*

Little is known about implementation. SPC is a routinely provided intervention in a number of healthcare systems, although the regularity of visits (3-4 times per year) may be a barrier for some patients (financial and logistical).

*Ethical Considerations*

No evaluation of equity or access to SPC has been conducted. However, utilisation of dental services is unequally distributed and therefore, it is reasonable to assume the same would be the case for SPC. Identifying barriers to and facilitators of SPC, and using this information to enhance access would seem to be a priority.

*Economic Considerations*

Limited evidence exists on the cost-effectiveness of SPC. SPC delivered in specialist care when compared with general dental practice may result in less CAL loss and higher tooth survival rates, but at a greater financial cost (Gaunt et al., 2008). Economic modelling indicates SPC is cost effective in developed economies (Pennington et al., 2011).

*Legal Considerations*

Not applicable.

**R11.2 | Does residual probing pocket depth, following active periodontal treatment, affect disease recurrence during SPC?**

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|---|
| PICOS question addressed by a SR  |
| R11.2 - Evidence-based statement  |
| <i>In patients with periodontitis, the presence of residual probing pocket depths (<math>\geq 5</math> mm) following active therapy increases the risk of disease recurrence/progression, even though the patient is enrolled in SPC.</i> |
| <b>Supporting literature</b> (Leow et al., 2021)  |
| <b>Quality of evidence</b> Moderate<br>Two studies, which were a prospective cohort, a controlled clinical trial with risk of bias designated as, 'low', and 'serious', respectively.   |
| <b>Grade of recommendation</b> Grade O – Statement: unclear, additional research needed   |
| <b>Strength of consensus</b> Unanimous consensus (0% of the group abstained due to potential Col)   |

## Background

### Intervention

The goals of supportive periodontal care (SPC) are to maintain periodontal stability (bleeding on probing in <10% of sites; shallow probing pocket depths of 4 mm or less, and no 4 mm sites with bleeding on probing) (Chapple et al., 2018), by preventing disease recurrence or progression and ultimately to prevent tooth loss. Ideally, patients enter SPC with periodontal stability, however in some situations the strict definition in the 2018 Classification of stability/health following periodontal treatment this is not always achieved. Residual periodontal probing depths (PPD)  $\geq 4$  mm with bleeding on probing are likely to be unstable and pose a risk for disease progression.

### Available evidence

#### *Number and design of included studies*

Two studies addressing disease recurrence (CAL loss  $\geq 2$  mm) during SPC were included, one controlled clinical trial and one prospective cohort.

#### *Risk of bias*

Study quality assessment using the Robins-I tool showed a 'serious' risk of bias and 'low' risk using the Newcastle-Ottawa scale.

#### *Effect sizes and their clinical relevance*

Based on one controlled clinical trial (Jenkins, Said, Radvar, & Kinane, 2000) patients with residual PPD  $\geq 6$  mm after active periodontal therapy (APT) demonstrated disease recurrence (CAL loss  $\geq 2$  mm) in the range of 20.5-28.6% of sites over 12-months follow up. In contrast, shallower residual PPD (4-5.9 mm) showed disease recurrence in the range of 11.6-11.8%. No statistically significant difference between groups was found with regard to the modality of treatment during SPC (coronal scaling versus subgingival instrumentation). The prospective cohort study (Cortellini, Buti, Pini Prato, & Tonetti, 2017) reported the highest rate of recurrence at sites PPD  $\geq 5$  mm (compared with PPD  $< 5$  mm) over a 20-year

period. Regression analysis showed that residual PPD significantly correlated with recurrence ( $p=0.0024$ ,  $R^2=0.31$ , Root Mean Square Error = 0.75).

### *Consistency*

Studies were heterogenous in design and reporting of outcomes. All studies describe increased disease recurrence with increasing residual probing pocket depth (PPD) after active periodontal therapy.

### *Balance of benefit and harm*

One study reported adverse events following subgingival instrumentation of residual pockets. These were however not deemed to be serious. An overall consideration of the benefit versus harm of achieving periodontal stability (no residual PPDs) following active periodontal treatment (APT) in order to reduce the risk of disease recurrence supports the strength of the statement.

### *Overall certainty of the evidence*

Moderate.

### *From evidence to recommendation- additional considerations*

#### *Acceptability*

Little is known about patient preferences in relation to periodontal stability at the completion of APT. Healthcare professionals have a strong preference for  $PPD \leq 4$  mm without bleeding on probing after completion of periodontal therapy.

#### *Feasibility*

Little is known about implementation. Direct and indirect costs of reaching periodontal stability at completion of periodontal therapy may be a barrier for some patients.

#### *Ethical and Legal Considerations*

Not applicable.

#### *Economic Considerations*

Limited evidence exists on direct/indirect costs of the treatment of disease recurrence during SPC. Clearly, disparities exist between countries, health-care systems and the modality of treatment chosen to treat the recurrence.

### R11.3 | Should recall intervals for SPC be guided by patients' risk status?

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|---|
| <b>Additional question raised by the WG</b>   |
| <b>R11.3 - Expert consensus-based recommendation</b>  |
| <i>We <b>recommend</b> that recall intervals for supportive periodontal care (SPC) should be guided by patients' risk profile as determined by individual risk factors (for example smoking, hyperglycemia) and disease-associated clinical measures (such as pocket depths and bleeding on probing).</i> |
| <b>Supporting literature</b> (Lang et al., 2015; Matuliene et al., 2008; Rosling, Serino, Hellstrom, Socransky, & Lindhe, 2001; Trombelli et al., 2015; Trombelli et al., 2017; Trombelli, Simonelli, Franceschetti, Maietti, & Farina, 2020) and Expert Opinion.   |
| <b>Quality of evidence</b> Not applicable   |
| <b>Grade of recommendation</b> Grade A – ↑↑   |
| <b>Strength of consensus</b> Unanimous consensus (0% of the group abstained due to potential Col)   |

### Background

#### Intervention

A patient's previous experience of periodontitis is a strong predictor of future disease activity in the absence or presence of periodontal treatment (Machtei et al., 1993; Martin, Page, Kaye, Hamed, & Loeb, 2009). Regular SPC is associated with reductions in tooth loss relative to irregular SPC (Saminsky, Halperin-Sternfeld, Machtei, & Horwitz, 2015). Risk factor control is an important element of the first step of therapy in the treatment of periodontitis (Ramseier et al., 2020; Sanz, Herrera, et al., 2020). It is important in an era of personalised dental medicine to determine whether frequency of SPC should be tailored according to a patient's risk profile. Patient risk profile can be estimated through different validated patient risk assessment tools, such as the PRA (Lang & Tonetti, 2003), the PRC/PreViser/DEPPA (Page, Martin, Krall, Mancl, & Garcia, 2003), PerioRisk (Trombelli et al.,

2017). Patient risk profile can also be expressed through the 'Grade' system (Tonetti et al., 2018).

### Available evidence

#### *Number and design of included studies*

In the systematic review (Leow et al., 2021), none of the studies that were included addressed risk factor control in SPC. No detail of factors that influenced frequency of the recall interval were given. One 12-year prospective cohort study (Rosling et al., 2001) evaluated disease progression in normal susceptibility (NS) and high susceptibility (HS) patients during 12-yrs of SPC, where SPC frequency was determined by risk/susceptibility categorisation at the end of active periodontal therapy.

#### *Risk of bias*

Not applicable.

#### *Effect sizes and their clinical relevance*

No included studies documented details on how risk factor control might have influenced recall intervals in SPC. Only one study (Rosling et al., 2001) included in the systematic review (Leow et al., 2021) investigated risk profiles in association with tooth loss, and suggested that tailoring frequency of SPC to risk profiles may prevent tooth loss in cohorts with different susceptibilities to periodontitis. Substantial evidence for the validity of different risk assessment tools based on individual risk factors (for example smoking, hyperglycemia) and disease-associated clinical markers (such as pocket depths and bleeding on probing) to predict tooth loss has been produced (Lang & Tonetti, 2003; Martin et al., 2009; Martin, Page, Loeb, & Levi, 2010; Matuliene et al., 2008; Page et al., 2003; Ramseier et al., 2019; Trombelli et al., 2017). Such tools may be used to inform the frequency of SPC recalls (Lang et al., 2015; Trombelli et al., 2020). Initial evidence suggests that 'Grading' (Tonetti et al., 2018) may be able to predict tooth loss (Al-Harathi, Barbagallo, Psaila, d'Urso, & Nibali, 2021; Ravida et al., 2020; Saleh et al., 2021) and may be used to set SPC frequency recalls, although more evidence is needed.

#### *Consistency*



Not applicable.

#### *Balance of benefit and harm*

Evidence suggests that the frequency of recall intervals for SPC may be set according to a patient's risk status, with high-risk individuals benefitting from 3-monthly SPC and lower risk patients remaining largely stable with a reduced frequency of 6-12 months. An overall consideration of the benefit versus harm of risk factor control to influence recall intervals of SPC supports the strength of the statement.

#### *Overall certainty of the evidence*

Not applicable.

#### *From evidence to recommendation- additional considerations*

##### *Acceptability*

Little is known about patients' preferences in relation to frequency of recall visits. Oral health care professionals are increasingly collaborating with other health care providers and health authorities to raise awareness of, and manage risk factors for the treatment of periodontitis.

##### *Feasibility*

Little is known about implementation of risk-driven recall intervals for SPC; however, experience of oral healthcare professionals suggests that 3-monthly SPC intervals are feasible and acceptable to patients at high risk of recurrence of periodontitis and associated tooth loss.

##### *Ethical Considerations*

Given the limited but consistent evidence that regular SPC is beneficial in reducing tooth loss and periodontitis progression or recurrence, it would seem appropriate to recommend more regular (3-4 monthly) SPC visits for those with a higher grade/risk of periodontitis than those with a lower grade/risk.

##### *Economic Considerations*

Some barriers may exist for patients at high risk due to the need for more frequent recall visits and the associated costs. This is likely to increase health inequalities in countries with no or limited public healthcare funding for periodontitis.

*Legal Considerations*

Not applicable.

**R11.4 | What are the important components to consider when designing a successful SPC programme?**

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|---|
| Additional question raised by the WG  |
| R11.4 - Expert consensus-based recommendation   |
| <i>We <b>recommend</b> a number of important components when designing an SPC programme, including:</i>   |
| <i>a. Specific interventions include, interview, assessment, evaluation, practical intervention and planning (see introduction).</i>  |
| <i>b. Delivery by a variety of oral healthcare professionals, under the supervision of a suitably trained general dentist or a specialist, as appropriate to case complexity.</i> |
| <i>c. Clear two-way communication between the oral healthcare team and the patient, and between healthcare professionals (medical or dental).</i>                                 |
| <b>Supporting literature</b> Expert Opinion.  |
| <b>Quality of evidence</b> Not applicable   |
| <b>Grade of recommendation</b> Grade A – ↑↑   |
| <b>Strength of consensus</b> Unanimous consensus (0% of the group abstained due to potential Col)   |

**Background**

*Intervention*

Supportive periodontal care (SPC) is the fourth step of therapy (Sanz, Herrera, et al., 2020). It is a complex intervention that elicits key questions relevant to both oral healthcare providers and patients and is crucial to the long-term stability of the periodontium.

Important aspects of SPC are documented below:

- a) Specific interventions to include in a SPC programme.

In designing an SPC programme, it is important to regularly consider a number of components which include:

- **Interview:** elicit information on periodontal health symptoms, medical and social history, risk factors including tobacco use, stress, diabetes and reported plaque control regime, patient motivation toward continuous risk factor control and professional mechanical plaque removal (PMPR)/ subgingival instrumentation;
- **Assessment:** plaque and calculus deposits, periodontal health including inflammation, probing pocket depths, and bleeding pockets;
- **Evaluation:** of intervention needs, including risk factor management, oral hygiene and re-treatment;
- **Communicating:** findings to patients to enhance their ownership of periodontal health and agreement on required interventions
- **Practical Intervention:** oral hygiene coaching, instrumentation of supra- and sub-gingival plaque and calculus, treatment of sites with recurrence or residual periodontitis.
- **Planning:** interval before next SPC visit.

b) The specific oral healthcare professional that undertakes/oversees the SPC programme

A variety of qualified and trained oral healthcare professionals can carry out the components of an SPC programme. Nine prospective cohort studies included in the systematic review (Leow et al., 2021) utilised undergraduate dental students, dental hygienists and periodontists.

The SPC programme should be overseen by a suitably qualified and trained general dentist or specialist. Effective communication is essential should the operator carrying out the components of the SPC programme differ from the person overseeing the SPC programme.

c) Key communication steps to undertake for long-term patient benefit?

- Oral healthcare professionals and the patient: communication between oral healthcare professionals delivering the SPC programme and the patient is crucial at each visit. The patient should have a clear understanding of his/her periodontal status, treatment needs (if any) and the recommended home-care regime.
- Communication between healthcare professionals: the person overseeing the SPC programme may be different to that delivering the components of an SPC programme. Clear and transparent communication between these oral healthcare professionals

should occur at each recall visit. Importantly, a number of healthcare professionals may be involved with a patient's care, particularly with regard to medical health and/or risk factor management. In order to work synergistically for long-term patient benefit, the person overseeing the SPC programme should initiate and maintain communications.

- Oral healthcare professional overseeing the SPC programme and the patient: the person overseeing the SPC programme should communicate with the patient on a regular basis. Patients should be actively engaged in the decision-making process regarding long-term care.

### Available evidence

#### *Number and design of included studies*

None of the studies included addressed specific components that should be included in an SPC programme, who should undertake or oversee the SPC programme nor which key communications steps should be undertaken for long-term patient benefit.

#### *Risk of bias, Effect sizes and their clinical relevance, Consistency, Balance of benefit and harm*

Not applicable.

### Overall certainty of the evidence

Not applicable.

### From evidence to recommendation- additional considerations

#### *Acceptability*

Little is known about patient preferences with regard to design and delivery of SPC programmes. Clear and transparent communication between healthcare professionals and with the patient is essential for long-term patient benefit.

#### *Feasibility, Ethical, Economic, Legal Considerations*

Not applicable.

**R11.5 | What is the best approach, when treating the recurrence of periodontitis during SPC to reduce tooth loss and/or influence other outcomes (e.g. measures of periodontal health, quality of life, cost and accessibility of care and harms)?**

|   |
|---|
| PICOS question addressed by a SR  |
| R11.5 - Evidence-based recommendation   |
| <i>We <b>suggest not</b> to use adjunctive approaches to subgingival instrumentation when treating recurrence of periodontitis during supportive periodontal care.</i>  |
| <b>Supporting literature</b> (Leow et al., 2021)  |
| <b>Quality of evidence</b> Moderate<br>Nine studies (7 randomised controlled trials, 1 controlled clinical trial and 1 prospective cohort) with ≥ 12 months follow-up. Risk of bias – 6 ‘of some concern’, 1 ‘high’, 2 ‘serious’. |
| <b>Grade of recommendation</b> Grade B - ↓  |
| <b>Strength of consensus</b> Consensus (0% of the group abstained due to potential CoI)   |

**Background**

Intervention

Periodontitis may become unstable during long-term SPC and may present as disease recurrence, occurrence or progression.

- Recurrence refers to a finding of periodontitis at a site that was rendered periodontally healthy/ stable through active treatment;
- Occurrence refers to a diseased site arising within a periodontitis patient that did not previously exhibit signs of disease;
- Progression is characterized by deterioration (e.g. clinical attachment loss) at a site that exhibited residual disease despite active treatment.

It may be challenging to distinguish between these, particularly if the SPC programme has not been continuously delivered in a single dental practice/office setting. Sites with probing pocket depths ≥ 4 mm and bleeding on probing require further treatment in order to reduce the risk of further deterioration and/or tooth loss.

Available evidence

*Number and design of included studies*

Nine studies with  $\geq 12$  months follow-up were included. Seven studies were RCTs, one study was a controlled clinical trial and one study was a prospective cohort.

Tooth Loss: two studies (one RCT and one prospective cohort) reported on tooth loss. These studies were reported qualitatively.

Clinical Attachment Level (CAL) loss  $\geq 2$  mm: two studies reported on CAL loss  $\geq 2$ mm (one RCT and one controlled clinical trial) and were included in the qualitative analysis.

Pockets of  $\geq 5$  mm with bleeding on probing: no studies reported on the number of PPD  $\geq 5$  mm with bleeding on probing during SPC.

Sites that need/experience re-treatment: one study (split mouth RCT) reported on breakdown sites which required re-treatment.

Patient reported outcomes: one RCT reported on oral health-related quality of life utilising the Italian translation of the Oral Health Impact Profile (OHIP) questionnaire -14.

Health economic outcomes: two RCTs provided information on total cumulative costs for operative interventions.

Other patient reported outcomes: a number of studies reported on other outcomes/adverse events. These included periodontal abscess (one RCT), masticatory function and aesthetics (one RCT) and adverse events (one controlled clinical trial and an RCT).

### *Risk of bias*

Nine studies were included. Study quality assessment using the Cochrane Risk of Bias Tool 2.0 showed six studies were of, 'some concern', and one study was classed as, 'high'. Two studies were judged as, 'serious' using the Robins-I tool.

### *Effect sizes and their clinical relevance*

Tooth Loss: one RCT (Bogren et al., 2008) on 128 patients with 3-year outcomes, compared subgingival instrumentation (SRP) alone (control) with SRP and locally delivered 8.8% doxycycline gel applications (test) in PPD  $\geq 5$  mm. SPC was conducted every 6 months. 25 test sites were lost due to tooth extractions (3.6% of initially included sites) in the test group, whilst 45 sites were lost due to extractions (4.9% of those initially included) in the control group. The difference between groups was not statistically significant ( $p > 0.05$ ). A prospective cohort (Costa et al., 2015), which included 212 patients, assessed surgical

therapy (ST) versus non-surgical therapy (NST) in both compliant (RC) and non-compliant patients (IC), over 5 years of follow-up. Whilst mean tooth loss for RC was significantly less [0.3 (NST) and 0.8 (ST)] than for IC [2.2 (NST) and 2.8 (ST)], no statistically significant difference was noted overall between ST and NST.

Clinical Attachment Level (CAL) loss  $\geq 2$  mm: one controlled clinical trial (Jenkins et al., 2000) compared coronal scaling (CS) in 17 patients (146 sites) with subgingival scaling (SS) in 14 patients (130 sites) over 12 months, and 21 sites exhibited CAL loss  $\geq 2$  mm from each group over the course of SPC, with no statistically significant differences between groups. A 12-month multi-centre RCT (Tonetti et al., 2012) on 202 subjects compared SRP (control) with SRP and 14% doxycycline gel application (test) on PPD  $\geq 5$  mm with bleeding on probing. 8 test and 7 control patients experienced CAL loss  $\geq 2$  mm with no statistically significant difference between the groups.

Sites that need/experience re-treatment: one split mouth RCT (Kaldahl, Kalkwarf, Patil, Molvar, & Dyer, 1996b) reported 685 'breakdown' sites during the course of SPC which required re-treatment. 5%-12% of these breakdown sites experienced CAL loss  $\geq 3$  mm and were re-treated and subsequently experienced further loss of attachment.

Patient reported outcomes: the Italian translation of the OHIP-14 questionnaire was used in one RCT (Cortellini, Stalpers, Mollo, & Tonetti, 2020) at baseline, 1, 5 and 10 years after regenerative treatment (other treatment groups were not relevant to this review). The mean OHIP-14 score one year after the regenerative procedure was 6.6 ( $\pm 2.4$ ), however no data was presented at 10 years.

Health economic outcomes: one RCT (Cortellini et al., 2017) reported cumulative costs over a 20-year period (with 3-monthly SPC) using an average of fees from private practices in Italy. The cumulative costs ranged from a mean of €3090.98 ( $\pm 210.66$ ) to €3382 ( $\pm 88.95$ ) and were dependent on the treatment carried out during the active phase of therapy. Another study (Cortellini et al., 2020) reported cumulative costs for a regenerative procedure over 10 years (excluding SPC).

Other patient reported outcomes: twenty-seven periodontal abscesses were reported in one RCT (Kaldahl, Kalkwarf, Patil, Molvar, & Dyer, 1996a) with 84 months of follow-up, with most (85%) occurring in the group originally treated by coronal scaling alone and a large proportion (63%) occurring in sites with PPD $\geq$  7 mm at the initial examination. (Cortellini et al., 2020) assessed masticatory function and aesthetics using a 5-point Likert scale with a 10-year follow-up, and the proportion of people reporting ‘some concern’ for both masticatory function and aesthetics appeared to increase over the 9 years of SPC (graphical information available only).

Adverse events were largely not described, but often judged as ‘not serious’ in two studies (Jenkins et al., 2000; Tonetti et al., 2012). Both studies reported no difference between study groups in regard to adverse events.

#### *Consistency*

Not applicable.

#### *Balance of benefit and harm*

The best approach to treatment of recurrence of periodontitis in SPC is currently unknown. However, as demonstrated in those studies included, some clinical benefit can be achieved regardless of treatment modality. Additionally, no difference between treatment approaches could be determined with respect to adverse events.

#### *Overall certainty of the evidence*

Low.

#### *From evidence to recommendation- additional considerations*

##### *Acceptability*

Little is known about patient preferences in regard to treatment of recurrence in SPC. Determining the best approach to treatment of recurrence in conjunction with patients’ views on these should undoubtedly be a research priority.

##### *Feasibility, Ethical, Legal Considerations*



Not applicable.

### *Economic Considerations*

The costs and cost effectiveness of re-treatment of recurrence are currently unknown.

**11.3 | Is regular, professionally administered, SPC associated with positive and/or negative outcomes, aside from tooth loss and/or disease recurrence?**

**R11.6 | Are there disadvantages to regular long-term SPC (e.g. more gingival recession/clinical attachment loss)?**

|  |
|--|
| <b>PICOS question addressed by a SR</b>  |
| <b>R11.6 - Evidence-based statement</b>  |
| <i>There is no evidence of clinical disadvantages to regular long-term SPC, such as gingival recession/ clinical attachment loss, however the possibility of these side effects cannot be excluded based on the evidence reviewed. Patients should be advised of this as part of their informed consent.</i> |
| <b>Supporting literature</b> (Leow et al., 2021)   |
| <b>Quality of evidence</b> Three prospective cohorts with a 'low' risk of bias.  |
| <b>Grade of recommendation</b> Grade O – Statement: unclear, additional research needed  |
| <b>Strength of consensus</b> Strong consensus (0% of the group abstained due to potential Col)   |

## **Background**

### Intervention

Periodontitis patients in long-term SPC should attend regular recall appointments in order to reduce their risk of tooth loss. At times, periodontitis may become unstable and require re-treatment which may take the form of a non-surgical and/or surgical approach to resolve probing pocket depths (PPD)  $\geq 4$  mm with bleeding on probing. One common consequence of re-treatment may be clinical attachment loss in the form of gingival recession, the magnitude of which is difficult to predict.

### Available evidence

### *Number and design of included studies*

Three prospective cohort studies contributed data to the meta-analysis for estimating the number of patients experiencing CAL loss  $\geq 2$  mm (86 participants) during SPC.

### *Risk of bias*

All three studies were classed as having, 'low' risk of bias using the Newcastle-Ottawa scale.

### *Effect sizes and their clinical relevance*

The primary outcome of the systematic review (Leow et al., 2021) was tooth loss. The secondary outcome, to inform on disease recurrence/progression, was CAL loss  $\geq 2$  mm. 'Regular' SPC was defined as 3-monthly, whilst a lack of adherence to or no SPC was described as 'irregular'. The mean proportion of patients who experienced overall CAL loss  $\geq 2$  mm was 24.8% (95% CI 11%-38%) with substantial heterogeneity  $I^2=63%$  ( $p=0.013$ ).

30.2% (95% CI -2%-63%) of patients who attended regular SPC appointments experienced CAL loss  $\geq 2$ mm, compared to 21.4% (95% CI 10%-33%) of those who attended irregularly. The difference between subgroups was not statistically significant ( $p=0.332$ ).

Although it appears that regular SPC does not lead to significantly greater experience of CAL loss  $\geq 2$ mm, this should be interpreted with caution. Only a small number of studies ( $n=3$ ) contributed to the meta-analysis and the resulting data for the regular SPC group appears imprecise (large confidence interval). Furthermore, the disparity may be explained by a single outlier where participants in that group presented with an increased number of residual PPD at the start of SPC.

A greater length of follow-up ( $\geq 10$  years) was associated with a slight increase in CAL loss  $\geq 2$  mm of 26.3% (95% CI 8%-45%) compared with 22.1% (95% CI 5%-39%) for 5-10 years follow-up.

### *Consistency*

Heterogeneity for studies included to inform on CAL loss  $\geq 2$  mm was substantial [ $I^2=63%$  ( $p=0.013$ )].

### *Balance of benefit and harm*

The desirable effects of long-term regular SPC (reduced prevalence of tooth loss) would undoubtedly outweigh possible undesirable effects regarding clinical attachment level. An overall consideration of the benefit versus harm of regular SPC supports regular SPC.

Overall certainty of the evidence

Low.

From evidence to recommendation- additional considerations

*Acceptability, Feasibility, Ethical, Economic, Legal Considerations*

See recommendation R11.1

*Legal Considerations*

Not applicable.

**R11.7 | Is long-term SPC cost effective when considering direct and indirect costs?**

|   |
|---|
| <b>Additional question raised by the WG</b>   |
| <b>R11.7 - Expert consensus-based statement</b>   |
| <i>We suggest that regular long-term SPC in specialist practice may result in greater periodontal stability and tooth survival when compared with SPC in general practice. We <b>do not know</b> if long-term SPC is cost effective when considering direct and indirect costs.</i> |
| <b>Supporting literature</b> (Gaunt et al., 2008) and Expert Opinion  |
| <b>Quality of evidence</b> Not applicable   |
| <b>Grade of recommendation</b> Grade O – Statement: unclear, additional research needed   |
| <b>Strength of consensus</b> Unanimous consensus (0% of the group abstained due to potential Col)   |

**Background**

Intervention

Costs incurred by SPC are complex and include both direct and indirect costs. Direct costs include elements such as the recall visits themselves and/or costs of re-treatment, whilst the consequences of periodontitis (e.g. cost of oral rehabilitation following tooth extraction

or root caries) and time commitments from the patient (i.e. absenteeism from work) are considered indirect costs. There are also “intangible” costs such as impact on quality of life and number of healthy life years.

### Available evidence

#### *Number and design of included studies*

No studies reported on direct, indirect and intangible costs in SPC.

#### *Risk of bias*

Not applicable.

#### *Effect sizes and their clinical relevance*

One systematic review (Gaunt et al., 2008) concluded that SPC delivered in a specialist environment led to greater periodontal stability (clinical attachment) and higher tooth survival rates when compared with general practice, but was more expensive to deliver (direct costs) in the specialist environment. The systematic review conducted an analysis on cost-effectiveness based on data from one study (Axelsson & Lindhe, 1981) extrapolated over a 30-year period. The analysis was from the perspective of a single patient with the primary patient-based outcome of tooth loss and secondary outcome of clinical attachment loss. The authors calculated ‘tooth years lost’, which considered time as a factor. Thus, one tooth lost after the first year of SPC, equated to 30 tooth years lost over the course of the evaluation. The comparison was taken for those patients who received SPC in specialist care (charges based on one specialist practice in North East England) versus in a general dental practice (charges based on State Health Service charges in Scotland). Importantly, this model assumed that only SPC would be undertaken (no periodontal re-treatment) and highlights the uncertainty in the values used in the analysis. An incremental cost effectiveness ratio (ICER) was created by considering the increase in cost of a particular programme (i.e. specialist or general dentist in either setting) by the increase in benefit (outcome). The results of the analysis showed that SPC when provided in specialist practice was more effective than that delivered by a general practitioner, in terms of tooth loss and clinical attachment. SPC in specialist practice however costs €4,466 more than a general dentist in private practice, and €5,938 more than a general dentist in a state health service

system. The ICER for SPC delivered in specialist care (general dentist in private practice as baseline) was €217 for one extra tooth year or an extra €1,130 for 1mm less attachment loss. When using the general dentist in a state-supported health service as a baseline, specialist care equated to €288 for one extra tooth year or an extra of €1,503 per 1mm loss of attachment. Undoubtedly, compliance with recall appointments and efficiency and appropriateness of care, is crucial to our understanding of cost-effectiveness. No data on compliance was given for the cohort of patients who received SPC in general practice.

*Consistency, Balance of benefit and harm*

Not applicable.

*Overall certainty of the evidence*

Very low.

*From evidence to recommendation- additional considerations*

*Acceptability*

It is unknown whether patients prefer SPC appointments in the specialist environment or in general practice. Often, a shared responsibility exists (between specialist and general dental practices) which may reduce overall costs possibly at the expense of tooth or clinical attachment loss.

*Feasibility*

Not applicable.

*Ethical Considerations*

Limited evidence exists that regular SPC is beneficial to the patient (reducing tooth loss and disease progression/ recurrence). Although SPC delivered in specialist practice appears to increase tooth survival and reduce clinical attachment loss when compared with general practice, this comes at a higher cost, which may be a barrier for some patients.

*Economic Considerations*

Limited evidence of the cost-effectiveness of SPC regarding direct and indirect costs exists and should be a clear future research priority.

### *Legal Considerations*

Not applicable.

## **R11.8 | Does long-term SPC impact upon patient-reported outcomes (PROs) (OHRQoL, masticatory function, aesthetics)?**

|   |
|---|
| <b>PICOS question addressed by a SR</b>   |
| <b>R11.8 - Evidence-based statement</b>   |
| <i>We <b>do not know</b> if long-term SPC impacts upon patient-reported outcomes.</i>             |
| <b>Supporting literature</b> (Leow et al., 2021)  |
| <b>Quality of evidence</b> Three prospective cohorts  |
| <b>Grade of recommendation</b> Grade O – Statement: unclear, additional research needed           |
| <b>Strength of consensus</b> Unanimous consensus (0% of the group abstained due to potential Col) |

### **Background**

#### Intervention

The impact of a disease and its treatment on a patient’s quality of life may be captured by patient-reported outcomes (PROs). A number of tools have been utilised to assess PROs, often in the form of questionnaires or scales. Periodontitis has been demonstrated to have a negative impact on a patient’s oral health-related quality of life (OH-QOL), whilst non-surgical therapy and surgical therapy may improve this (Shanbhag, Dahiya, & Croucher, 2012), using validated PRO measures.

#### Available evidence

##### *Number and design of included studies*

Three prospective cohorts reporting on PROs were included.

##### *Risk of bias*

All three studies were judged as, 'low' risk of bias using the Newcastle-Ottawa scale.

#### *Effect sizes and their clinical relevance*

Patient reported outcomes: the Italian translation of the OHIP-14 questionnaire was used in one RCT (Cortellini et al., 2020) at baseline, 1, 5 and 10 years after regenerative treatment (other treatment groups were not relevant to this review). The mean OHIP-14 score one year after the regenerative procedure was 6.6 ( $\pm 2.4$ ). However, no data were presented at 10 years.

Other PROs: twenty-seven periodontal abscesses were reported in one RCT (Kaldahl et al., 1996a), with 84 months of follow-up, with most (85%) occurring in the group originally treated by coronal scaling alone and a large proportion (63%) occurring in sites with PPD $\geq$ 7 mm at the initial examination.

(Cortellini et al., 2020) assessed masticatory function and aesthetics using a 5-point Likert scale with a 10-year follow-up. The proportion of people reporting 'some concern' for both masticatory function and aesthetics appear to increase over the 9 years of SPC (graphical information available only).

#### *Consistency*

Not applicable.

#### *Balance of benefit and harm*

Regular SPC is of benefit of the patient to reduce the risk of tooth loss and clinical attachment loss, whilst limited evidence exists on PROs.

#### *Overall certainty of the evidence*

Low.

#### *From evidence to recommendation- additional considerations*

*Acceptability, Feasibility, Ethical, Economic, Legal Considerations*

Not applicable.

## 12 | IMPACT OF TREATMENT ON SYSTEMIC HEALTH AND QUALITY OF LIFE

### 12.1 | Intervention – Periodontal treatment: impact on systemic health and quality of life

A systematic review (Orlandi et al., 2021) addressed the impact of periodontal interventions [various methods including non-surgical (steps 1 and 2), surgical (step 3) and adjunctive therapies] on systemic health and quality of life in patients with severe periodontitis who:

- 1) were systemically healthy by anamnesis (medical history);
- 2) exhibited one or more co-morbid systemic non-communicable diseases (NCDs);
- 3) were pregnant.

NCDs assessed were: cardiovascular diseases, arrhythmias (AF), hypertension, rheumatic, neurological, respiratory, metabolic, kidney, liver and inflammatory gastrointestinal (GI) diseases, malignancy, osteoporosis and mental health conditions (G.B.D. Diseases and Injuries Collaborators, 2020).

The included intervention studies did not specifically provide treatment to patients to a defined endpoint/outcome of success, therefore there may be an underestimation of the effect size upon the systemic outcomes defined by the PICOS. Furthermore, treatment of periodontitis is instigated for the purpose of improving oral health, and systemic health benefits in patients without a co-morbid NCD are therefore a secondary consideration because an absence of any beneficial systemic effect would not contraindicate the periodontal therapy. Whilst the most relevant analysis refers to the treatment of periodontitis in patients with co-morbid NCDs (n=29 RCTs), data were also combined with that from systemically healthy individuals (n=3 RCTs). This approach was not defined *a priori* and it represents a methodological limitation of the review, but it was deemed to be justified on the basis that there would likely be patients within the systemically healthy group who had undiagnosed NCDs.

Sixteen RCTs addressed adverse pregnancy outcomes (preterm birth <37, <35, and <32 weeks, low birth weight <2500 gr and <1500 gr, preterm low birth weight, pre-eclampsia,



gestational age at delivery, C-reactive protein (CRP), stillbirth, birthweight, and perinatal loss).

Following an update of the systematic search, five new studies were identified (Buwembo et al., 2020; Montero et al., 2020; Nguyen et al., 2021; Qureshi, Bokhari, Haque, Baloch, & Zaheer, 2021; Rapone et al., 2021) with data from four of them included in meta-analyses (Montero et al., 2020; Nguyen et al., 2021; Qureshi et al., 2021; Rapone et al., 2021). The updated meta-analyses did not change the interpretation of the available evidence apart from the increase in diastolic blood pressure previously observed for PICOS #2 which became non-statistically significant [0.15 mmHg 95% confidence interval -CI (-0.14, 0.44) p=0.311]. Furthermore, a statistically significant reduction in tumour necrosis factor (TNF)-α [-0.27 pg/ml 95% CI (-0.53, 0.014) p=0.039] was observed for PICOS #1 and PICOS #2 populations combined.

**12.1.1 | Impact of periodontal treatment on systemic inflammation and cardio-metabolic risk in people with no reported systemic co-morbidity (presumed systemically healthy)**

**R12.1 | Does periodontal treatment have an impact on systemic inflammation and cardio-metabolic risk in people with no reported systemic co-morbidity (presumed systemically healthy)?**

|   |
|---|
| PICOS question addressed by a SR  |
| R12.1 - Evidence-based statement  |
| <i>Treatment of periodontitis <b>may</b> improve levels of biomarkers of systemic inflammation and cardiometabolic risk in people with no reported systemic co-morbidity.</i> |
| <b>Supporting literature</b> (Orlandi et al., 2021)   |
| <b>Quality of evidence</b> Low - Three RCTs at low risk of bias   |
| <b>Grade of recommendation</b> Grade O – Statement: unclear, additional research needed   |
| <b>Strength of consensus</b> Strong consensus (2.1% of the group abstained due to potential Col)  |

**Background**

Intervention

Treatment of periodontitis consisted of step one (behaviour change, oral hygiene coaching and supra-gingival professional mechanical plaque removal (PMPR), step two (sub-gingival removal of dental biofilm and calcified deposits and use of adjunctive therapies), step three (surgical periodontal therapy) and step four (supportive periodontal care) in order to reduce gingival inflammation (Sanz, Herrera, et al., 2020). Observational evidence has linked periodontitis to increased risk of non-communicable diseases (NCDs) (Sanz et al., 2018; Sanz, Marco Del Castillo, et al., 2020). Multiple mechanisms have been proposed to explain the biological plausibility of a systemic effect of periodontitis (Hajishengallis & Chavakis, 2021). Furthermore, evidence from interventional data suggests that the treatment of periodontitis may have an impact on systemic health outcomes (D'Aiuto, Orlandi, & Gunsolley, 2013; Hajishengallis & Chavakis, 2021; Simpson et al., 2015).

#### Available evidence

##### *Number and design of included studies*

Three randomised controlled trials (Fu, Li, Xu, Gong, & Yang, 2016; Tonetti et al., 2007; Zhou et al., 2017) provided data on the effect of the treatment of periodontitis in comparison with no/control treatment on systemic health in systemically healthy participants with periodontitis. Systemic outcomes reported in these trials included high sensitivity C Reactive protein (hs-CRP), fasting plasma glucose, tumour necrosis factor (TNF)-alpha, interleukin 6 (IL-6), total cholesterol (TC), High Density Lipoprotein (HDL) cholesterol, Low Density Lipoprotein (LDL) cholesterol, triglycerides (TG), flow mediated dilatation (FMD), systolic blood pressure (SBP), diastolic blood pressure (DBP) and Body Mass Index (BMI) at 6 months follow-up. Meta-analyses were performed by systemic outcome for hs-CRP, IL-6, TC, HDL cholesterol, LDL cholesterol, TG, SBP, and DBP at 6 months.

##### *Risk of bias*

The three trials included in the analysis were considered at low risk of bias according to the ROB2 tool.

##### *Effect sizes and their clinical relevance*

Although reductions in systemic biomarkers of inflammation and metabolic control were reported, no statistically significant overall effect of periodontal therapy was observed after 6-months or more of follow-up.

#### *Consistency*

Meta-analysis of three studies showed a reduction in eight biomarkers (hs-CRP, IL-6, TC, HDL, LDL, TG, SBP and DBP) with high levels of heterogeneity in 6 meta-analyses and wide confidence intervals.

#### *Balance of benefit and harm*

No evidence of harm was reported in any of the clinical trials.

#### *Overall certainty of the evidence*

High.

#### *From evidence to recommendation- additional considerations*

##### *Acceptability*

Little is known about patient preferences in relation to the treatment of periodontitis, due to a paucity of patient-reported outcome data.

##### *Feasibility*

Little is known about the implementation of periodontal therapy that is targeted at reducing cardiovascular biomarkers or those targeted at lowering metabolic risk, predominantly because the primary purpose of periodontal treatment is to improve periodontal rather than systemic health outcomes. Treatment of periodontitis is routinely performed in many healthcare systems across the world, and therefore is in itself feasible for those who can afford care or those able to gain access to care. There are however groups in society who struggle to access periodontal care for various reasons, some being cost (The Economist Intelligence Unit, 2021).

##### *Ethical Considerations*

Evaluation of the efficacy of the treatment of periodontitis on systemic health outcomes is ethically challenging as it would entail comparison with no treatment.

#### *Economic Considerations*

Cost-effectiveness has not been evaluated in these studies.

#### *Legal Considerations*

Not applicable.

### **12.1.2 | Impact of periodontal treatment on systemic inflammation and cardio-metabolic risk in people with co-morbid systemic non-communicable disease (NCD)**

#### **R12.2 | Does treatment of periodontitis impact upon hard outcomes or complications of systemic NCDs, in periodontitis patients with a co-morbid NCD?**

|  |
|--|
| <b>PICOS question addressed by a SR</b>  |
| <b>R12.2 - Expert consensus-based statement</b>  |
| <i>It is currently unclear if the treatment of periodontitis improves hard outcomes or complications of systemic NCDs in patients with periodontitis with a co-morbid NCD.</i> |
| <b>Supporting literature</b> (Orlandi et al., 2021)  |
| <b>Quality of evidence</b> Very Low - One feasibility RCT at high risk of bias   |
| <b>Grade of recommendation</b> Grade O – Statement: unclear, additional research needed  |
| <b>Strength of consensus</b> Consensus (2.4% of the group abstained due to potential Col)  |

#### **Background**

##### Intervention

Treatment of periodontitis was exactly as described under R12.1.

##### Available evidence

###### *Number and design of included studies*

One randomised controlled study (feasibility trial) reported data on the effect of the treatment of periodontitis in comparison with no/control treatment on hard outcomes or complications in patients with a non-communicable disease (Beck et al., 2008).

### *Risk of bias*

The trial was considered at high risk of bias according to the ROB 2 tool.

### *Effect sizes and their clinical relevance*

No statistically significant overall effect of periodontal therapy on cardiovascular events was observed.

### *Consistency*

Not applicable.

### *Balance of benefit and harm*

No evidence of harm was reported in this study.

### *Overall certainty of the evidence*

Low.

### *From evidence to recommendation- additional considerations*

#### *Acceptability*

Little is known about patient preferences in relation to treatment of periodontitis in patients with a NCD.

#### *Feasibility*

Little is known about the implementation of periodontal treatment in patients with NCDs, or where periodontal therapy is prioritised by those patients relative to other co-morbidities within their overall healthcare portfolio. Treatment of periodontitis is routinely performed in many healthcare systems across the world, and therefore is in itself feasible, accepting the limitations outlined in R12.1.

#### *Ethical Considerations*

Evaluation of the efficacy of the treatment of periodontitis on systemic health outcomes is ethically challenging as it would entail comparison with no treatment or a delayed

treatment group, where adverse outcomes may arise in periodontal health, irrespective of systemic health outcomes.

*Economic Considerations*

Insufficient evidence exists on the cost-effectiveness of the treatment of periodontitis when evaluating hard outcomes of systemic disease and/or complications of systemic conditions.

*Legal Considerations*

Not applicable.

**R12.3 | Does periodontal treatment improve systemic inflammation, metabolic control and cardiovascular risk in periodontitis patients with a co-morbid NCD?**

|   |
|---|
| PICOS question addressed by a SR  |
| R12.3 - Evidence-based recommendation   |
| <i>We <b>suggest</b> that treatment of periodontitis is <b>performed</b> to reduce systemic inflammation, to reduce cardiovascular risk profile and to improve metabolic control in patients with co-morbid NCD, however treatment protocols should include careful consideration of the general health status of the patient (e.g. quadrant versus full-mouth approach).</i> |
| <b>Supporting literature</b> (Orlandi et al., 2021)   |
| <b>Quality of evidence</b> Moderate - Six RCTs were considered at high risk of bias, nine at moderate risk and 18 at low risk of bias   |
| <b>Grade of recommendation</b> Grade B - ↑  |
| <b>Strength of consensus</b> Consensus (0% of the group abstained due to potential Col)   |

**Background**

Intervention

Treatment of periodontitis was exactly as described under R12.1.

Available evidence

*Number and design of included studies*

Thirty-three randomised controlled trials reported data on the effect of the treatment of periodontitis in comparison with no/control treatment on systemic health in patients with a

non-communicable disease. Populations with type 2 diabetes, cardiovascular diseases, polycystic ovary syndrome (POS), end-stage renal disease (ESRD), multiple co-morbidities (MC), rheumatoid arthritis (RA), and chronic kidney disease n (CKD) were reported. Systemic outcomes evaluated included hs-CRP, TNF-alpha, IL-6, ESR, HbA1c, fasting plasma glucose, TC, HDL cholesterol, LDL cholesterol, TG, VLDL, FMD, BMI, SBP, DBP, pulse, sCR and albumin at 6 months follow-up. Meta-analyses were conducted by systemic outcome for hs-CRP, fasting plasma glucose, TNF-alpha, IL-6, TC, HDL cholesterol, LDL cholesterol, TG, FMD, SBP, DBP and BMI at 6-month follow-up and for hs-CRP, IL-6, HbA1c, TC, HDL cholesterol, Estimated Glomerular Filtration Rate (eGFR) and Asymmetric dimethylarginine (ADMA) at 12-month follow-up

#### *Risk of bias*

Out of thirty-three trials, six were considered at high risk, 9 at moderate risk and 18 at low risk of bias according to ROB 2.

#### *Effect sizes and their clinical relevance*

Treatment of periodontitis demonstrated a statistically significant reduction in hs-CRP (0.47 mg/l, 95%CI 0.20-0.74), reduction in fasting plasma glucose (1.07 mmol/l, 95%CI 0.25-1.89) and increase in FMD (0.31%, 95%CI 0.07-0.55) at 6-month follow-up.

#### *Consistency*

Fifteen out of sixteen clinical trials reported a reduction in serum hs-CRP but with high heterogeneity. Six out of eight studies reported a reduction in FPG but with high heterogeneity. Both of the studies investigating FMD as a primary outcome measure reported an increase in FMD with low heterogeneity.

No evidence of publication bias was observed.

Meta-analyses on IL-6 (6 studies), TNF- $\alpha$  (4 studies) and HbA1c (14 studies) reported statistically non-significant reductions following treatment of periodontitis.

#### *Balance of benefit and harm*

No evidence of harm was reported in any studies.

Overall certainty of the evidence

Moderate.

From evidence to recommendation- additional considerations

*Acceptability*

Little is known about patient preferences in relation to treatment of periodontitis in people with a co-morbid systemic condition, due to the lack of studies addressing patient-reported outcomes.

*Feasibility*

Little is known about implementation of protocols targeted at reducing systemic biomarkers of cardio-metabolic risk. Treatment of periodontitis is routinely performed in many healthcare systems across the world, and therefore is in itself feasible, accepting the limitations outlined in R12.1.

*Ethical Considerations*

The evaluation of the efficacy of the treatment of periodontitis on systemic health outcomes is ethically challenging for the reasons stated in R12.2.

*Economic Considerations*

Insufficient evidence exists on the cost-effectiveness of the treatment of periodontitis when evaluating biomarker or other surrogate outcomes of systemic disease and/or complications of systemic conditions.

*Legal Considerations*

Not applicable.

**12.1.3 | Does periodontal treatment reduce the risk of adverse pregnancy outcomes?**

**R12.4 | Does periodontal treatment during pregnancy reduce adverse pregnancy outcomes?**



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| PICOS question addressed by a SR   |
| R12.4 - Evidence-based statement   |
| <i>It is unclear whether treatment of periodontitis during pregnancy may reduce preterm births (&lt;37 weeks) or reduces other adverse pregnancy outcomes.</i> |
| <b>Supporting literature</b> (Orlandi et al., 2021)  |
| <b>Quality of evidence</b> Moderate - 3 RCTs were of high risk of bias, 10 studies were graded as moderate and the remaining 3 as low risk of bias.            |
| <b>Grade of recommendation</b> Grade O – Statement: unclear, additional research needed, specifically focussed on high-risk individuals.                       |
| <b>Strength of consensus</b> Strong consensus (0% of the group abstained due to potential Col)   |

## Background

### Intervention

Treatment of periodontitis was as described under R12.1. Epidemiological studies have shown that periodontal diseases increase the odds of several pregnancy complications with the strength of the associations varying depending upon the study population (Ide & Papapanou, 2013; Jeffcoat, Geurs, Reddy, Goldenberg, & Hauth, 2001; Offenbacher et al., 1996). Prevention strategies including oral hygiene instructions and supra/subgingival instrumentation of the dentition are encouraged during pregnancy to maintain/restore oral health. However, it is still unclear whether the treatment of periodontal diseases has an effect on preventing adverse pregnancy outcomes such as preterm birth or low birth weight.

Subgingival instrumentation has traditionally been delivered during multiple sessions (e.g. quadrant-wise). As an alternative, full-mouth protocols have been suggested. Full-mouth protocols included single stage and two-stage therapy within 24 hours, however protocols including adjunctive antiseptics (full-mouth disinfection) were not included in this analysis.

### Available evidence

#### *Number and design of included studies*

Sixteen RCTs reported on the effect of treatment of periodontitis on pregnancy outcomes. The pregnancy outcomes assessed in the meta-analysis comprised preterm birth <37, <35,

and <32 weeks, low birth weight <2500 g and less than <1500 g, preterm low birth weight, pre-eclampsia, gestational age at delivery, CRP, stillbirth, birthweight, and perinatal loss.

#### *Risk of bias*

Of the 16 studies, 3 were at high risk of bias, 10 studies were graded as moderate and the remaining 3 as low risk of bias based on the ROB 2 tool.

#### *Effect sizes and their clinical relevance*

Based on 14 RCTs, the treatment of periodontitis resulted in a statistically significant reduction of preterm births (<37 weeks) (0.77 risk ratio, 95% CI 0.60- 0.98).

#### *Consistency*

Nine out of fourteen RCTs resulted in a reduction of preterm births (<37 weeks).

#### *Balance of benefit and harm*

Of the studies included that reported adverse effects, none reported maternal mortality following non-surgical periodontal interventions. Clinicians should be aware that there is evidence of systemic consequences (e.g. acute-phase systemic inflammatory response and vascular dysfunction) with full-mouth protocols. Whilst the clinical relevance of such changes remains to be determined, such an approach should always include careful consideration of the general health status of the patient.

#### *Overall certainty of the evidence*

Moderate.

#### *From evidence to recommendation- additional considerations*

##### *Acceptability*

Little is known about patient preferences regarding the treatment of periodontitis during pregnancy, due to the lack of studies addressing relevant patient-reported outcomes.

##### *Feasibility*

Little is known about implementation protocols targeted at reducing adverse pregnancy outcomes. Treatment of periodontitis is routinely performed in many healthcare systems across the world, and therefore is in itself feasible, accepting the limitations outlined in R12.1.

#### *Ethical Considerations*

Evaluation of the efficacy of the treatment of periodontitis on adverse pregnancy outcomes is ethically challenging as it would entail comparison with no treatment or treatment delayed until post-partum. There is another potential ethical dilemma in that patient preference may conflict with the clinician's recommendation in terms of mode of treatment delivery or timing of treatment. Patient autonomy should be respected.

#### *Economic Considerations*

Insufficient evidence exists on the cost-effectiveness of the treatment of periodontitis when evaluating adverse pregnancy outcomes.

#### *Legal Considerations*

Not applicable.

## **12.2 | Intervention – Prosthetic rehabilitation in fully or partially edentulous patients: impact on systemic health and quality of life**

A systematic review (Gennai et al., 2021) explored the impact of treating partial or complete edentulism in patients with periodontitis and those with tooth loss from any cause, on oral health-related quality of life (OHR-QoL) and general health.

The review considered the impact of rehabilitation of edentulous spaces of 5 or more teeth, in order to identify patients with stage IV periodontitis. However, only 13 studies recorded data from periodontitis patients, and even in these studies the reasons for the tooth loss were not documented. Forty-three studies were available that met the criteria of analysing oral health quality of life outcomes and specific measures of general health (cognitive

impairment, nutritional status, frailty, systemic serum markers) in patients with edentulous spaces of 5 or more teeth.

The recommendations made by the workshop focussed on the available data from 13 studies of periodontitis patients. However, as periodontitis is a major cause of tooth loss in adults (overall prevalence 45-50% and severe periodontitis on 7-11%), data was also considered from 43 studies where the presence of periodontitis was not specified, on the assumption that it is likely to have contributed to tooth loss in a number of cases studied. This decision reflected the limitations of the available literature, but the guideline group endorsed the pragmatic approach.

OHR-QoL was analysed using various validated tools including: OHIP-14, OHIP-20, OHIP-49, OHIP-54, OHIP-EDENT, OHIP-EDENT-21, OHQoL-UK, OIDP, DIDL and GOHAI, and VAS, Likert scales or questionnaires for patient satisfaction (12 different methods). Quality of life instruments used to analyse general health status included EORTC QLQ-C30, EORTC QLQ-H&N35, GHQ, SIQ, SF-36, WHOQoL-BREF, GSS and EQ-5D (n=8).

**12.2.1 | In people with a minimum of 5 teeth missing for any reason (including stage IV periodontitis patients), does prosthetic rehabilitation of edentulous spaces improve quality of life?**

**R12.5 | Does prosthetic rehabilitation of partial edentulism improve quality of life in people with tooth loss (for any reason, including periodontitis)?**

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| PICOS question addressed by a SR  |
| R12.5 - Evidence-based recommendation (1), Evidence-based statements (2,3)  |
| <ol style="list-style-type: none"><li><b>1. We recommend</b> rehabilitation of people with partial edentulism of at least 5 teeth (including those affected by periodontitis) to improve quality of life.</li><li>Rehabilitation of partial edentulism with tooth-supported, fixed or removable prostheses improves quality of life.</li><li>Rehabilitation of partial edentulism with implant-supported prostheses improves quality of life.</li></ol> |
| <b>Supporting literature</b> (Gennai et al., 2021)  |

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| <b>Quality of evidence</b> Moderate  |
| <b>Grade of recommendation</b> Grade A – ↑↑  |
| <b>Strength of consensus</b> Strong consensus (1.9% of the group abstained due to potential Col) |

## Background

### Intervention

Partially edentulous spaces may be left un-restored or may be restored using a variety of approaches, including fixed or removable prostheses, which may or may not be supported by teeth or dental implants. Such restorations provide numerous benefits that are reported to provide positive impacts beyond the oral cavity including, but not limited to function and aesthetics. There is also a body of evidence suggesting improvements in quality of life following the restoration of partially edentulous spaces.

Oral health-related quality of life (OHRQoL) has been measured with psychometric questionnaires. Restoration of edentulous spaces appears to incur significant changes in OHRQoL and such changes appear tangible to those patients treated by such reconstructions.

### Available evidence

#### *Number and design of included studies*

The evidence underpinning this recommendation includes 5 RCTs (465 patients), one cross-sectional study, a case-control trial (14 patients) and one prospective case series (248 patients), with all studies consistently highlighting that the restoration of partial edentulism led to an improvement in quality of life.

#### *Risk of bias*

Risk of bias was evaluated via the Cochrane reviewers' Handbook for interventional studies identifying three studies at high risk of bias and three with moderate risk of bias. One case-control study was at low -risk of bias (5 stars out of 6) on the Newcastle Ottawa Scale.

### *Effect sizes and their clinical relevance*

Improvements were consistently statistically significant and the magnitude of improvement was superior to the 'minimally important difference' (MID) when available, suggesting clinically meaningful effect sizes.

There were no randomized studies evaluating treatment vs. no-treatment. Thus, pre-operative to post-operative differences were evaluated in order to assess the impact of the treatment protocol studied.

### *Consistency*

Overall, studies reported that restoration of partial edentulism with tooth-supported restorations led to an improvement in quality of life.

### *Balance of benefit and harm*

Benefits and harms were not reported, although it may be speculated that tooth-supported fixed restorations, may be associated with some potential harm due to complications associated with the endodontic and prosthodontic components of the treatment. In the case of implant-supported restorations, potential harms associated with implant placement (potential intra- and post-operative complications) and maintenance (especially in people affected by periodontitis showing higher risk of peri-implantitis and implant loss) should be carefully considered.

However, overall, the perceived benefits in terms of masticatory function and improvements in quality of life appear to exceed the potential harms.

### *Overall certainty of the evidence*

High (consistency and effect size) to Moderate (quality of the included studies).

### *From evidence to recommendation- additional considerations*

#### *Acceptability*

Restoration of edentulism is broadly accepted by both patients and institutions and widely requested by patients.

#### *Feasibility*

Approaches to restoring edentulous spaces vary according to the knowledge and skills of individual dental practitioners, dental practice/office protocols, and healthcare funding systems which vary widely from country to country. There appear to be challenges however for frail populations and the elderly living in care homes. Moreover, surgical options are not universally available, and may reflect healthcare funding and the financial circumstances of individuals, thereby also reflecting health inequalities.

*Ethical Considerations*

Many national health systems cover/reimburse the costs for treatment of edentulism. However, in some countries fees for treatment are borne entirely by the individual patient.

*Economic Considerations*

The costs associated with the restoration of edentulous spaces vary widely according to the type of restoration provided, with removable options (removable dental prostheses) generally costing significantly less than fixed restorations (tooth/implant-supported fixed partial dental prostheses).

*Legal Considerations*

Not applicable.

**R12.6 | Does provision of conventional complete removable prostheses, in one or in both dental arches, improve quality of life in fully edentulous patients when compared with no rehabilitation?**

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| PICOS question addressed by a SR  |
| R12.6 - Evidence-based recommendation   |
| <i><b>We recommend</b> providing complete conventional removable prostheses to treat fully edentulous patients (including those who have lost teeth due to periodontitis), in one or both arches, to improve quality of life.</i> |
| <i><b>Supporting literature</b></i> (Gennai et al., 2021)   |
| <i><b>Quality of evidence</b></i> Moderate  |
| <i><b>Grade of recommendation</b></i> Grade A – ↑↑  |

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| <b>Strength of consensus</b> Strong consensus (0% of the group abstained due to potential Col) |
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## Background

### Intervention

The traditional approach to treating complete edentulism involves rehabilitation with complete removable prostheses. Overall, this approach to treatment is technically less demanding, universally accessible and associated with lower costs than implant-supported overdentures.

### Available evidence

#### *Number and design of included studies*

The evidence supporting this recommendation is based on a systematic review and meta-analysis (Gennai et al., 2021), 44 studies, of which 8 were interventional and 36 observational.

#### *Risk of bias*

Risk of bias was evaluated through the Cochrane reviewers' Handbook for interventional studies and the Newcastle Ottawa Scale for observational studies. Overall studies were judged to be at moderate to high risk of bias and none of the manuscripts included were found to be at low risk of bias. Interventional studies were judged to be at moderate to high risk of bias as these studies showed on average 45% of items that were considered adequate. The observational studies showed 57% of items judged positively, thereby indicating a moderate overall risk of bias.

#### *Effect sizes and their clinical relevance*

The effect measured through psychometric questionnaires was both statistically significant and clinically meaningful as significant changes of GOHAI, OHIP-14 and OHIP-49 were noticed after rehabilitation.

The magnitude of the effect is considered relevant for the patient if superior, on average, to the value of minimally important difference (Tsakos, Allen, Steele, & Locker, 2012).



### *Consistency*

There is a high level of consistency throughout the selected studies. None of the studies reported an absence of effect. Indeed, all the studies reported significant improvements in the various psychometric questionnaires used.

### *Balance of benefit and harm*

Harms associated with treatment of edentulism with conventional full removable dental prostheses are negligible. Patients may have temporary difficulties in adapting to new prostheses. Moreover, poorly fitting removable prostheses may be a cause of discomfort.

### *Overall certainty of the evidence*

High.

### *From evidence to recommendation- additional considerations*

#### *Acceptability*

Conventional removable dental prostheses are traditionally the most commonly used method of rehabilitation for fully edentulous patients. In general, they are safe and effective and the positive changes in quality of life reported improve their acceptability. In some patients however, the movement associated with the prosthesis may constitute an important psychological issue.

#### *Feasibility*

Conventional removable dental prostheses are routinely provided by dentists worldwide. The design and provision of conventional removable dental prostheses is practical, time-effective and safe. Importantly, the relatively modest costs associated with this type of rehabilitation significantly inform its feasibility.

#### *Ethical Considerations*

Not applicable.

#### *Economic Considerations*

Conventional removable dental prostheses are the least expensive form of treatment to rehabilitate fully edentulous patients. Many national health systems cover/reimburse the costs of treating edentulism. However, in some countries, treatment fees may have to be borne entirely by the patient.

*Legal Considerations*

Not applicable.

**R12.7 | Are implant-supported full-arch removable dental prosthesis (overdenture) superior to conventional full-arch removable prostheses in terms of improvement of quality of life?**

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| Additional question raised by the WG   |
| R12.7 - Expert consensus-based recommendation  |
| <i><b>We suggest</b> treating fully edentulous people (including those affected by periodontitis) with implant-supported full-arch removable dental prosthesis (overdenture), rather than conventional full-arch removable prostheses, to improve quality of life.</i> |
| <i><b>Supporting literature</b></i> (Allen et al., 2006; Awad, Locker, Korner-Bitensky, & Feine, 2000; Harris et al., 2013; Heydecke, Thomason, Lund, & Feine, 2005; Muller et al., 2013), included in the systematic review (Gennai et al., 2021)                     |
| <i><b>Quality of evidence</b></i> Moderate   |
| <i><b>Grade of recommendation</b></i> Grade B – ↑  |
| <i><b>Strength of consensus</b></i> Unanimous consensus (14.6% of the group abstained due to potential Col)  |

**Background**

*Intervention*

Implant-supported full-arch removable dental prostheses (overdentures) are frequently advocated to overcome complications associated with conventional full-arch removable prostheses, such as fit, aesthetics and masticatory function.

*Available evidence*

*Number and design of included studies*

The evidence for this recommendation is based on four RCTs (3 cohorts, 342 patients) evaluating implant-supported full-arch overdentures versus conventional removable prostheses in fully edentulous patients. Quality of life was evaluated through OHIP-49 and social impact questionnaires.

#### *Risk of bias*

Risk of bias was evaluated through the Cochrane reviewers' Handbook for interventional studies identifying two studies at high risk of bias and two with moderate risk of bias.

#### *Effect sizes and their clinical relevance*

Differences in outcome appear socially meaningful and statistically relevant.

#### *Consistency*

Three studies reported significantly greater improvements in quality of life for patients treated with implant-supported overdentures.

#### *Balance of benefit and harm*

Benefits and harms were not reported, although it is plausible that implant placement may be associated with some potential harms. Implant placement procedures may be associated with potential intra- and post-operative complications. Moreover, implants, especially in people affected by periodontitis show higher risk of developing peri-implantitis and implant loss.

#### *Overall certainty of the evidence*

Moderate.

#### *From evidence to recommendation- additional considerations*

##### *Acceptability*

Restoration of edentulism is widely advocated and accepted. However, some patients may not be willing to undergo a surgical procedure for implant placement.

##### *Feasibility*

The restoration of edentulous spaces using implant-supported restorations is widely undertaken. However, in certain situations access to surgical treatment may be limited as surgical facilities and skills may not be present in every dental setting. Furthermore, there are a high number of national healthcare systems that do not provide implant treatments. Moreover, implants require supportive maintenance care in all patients, but especially in those previously affected by periodontitis, which may not always be accessible.

#### *Ethical Considerations*

The fact that dental implant-supported overdentures are more expensive than conventional removable prostheses may raise some ethical concerns as there may be a gradient of improvement of OHRQoL related to the affordability of the procedure, thereby impacting adversely upon social inequalities.

#### *Economic Considerations*

Restoration of edentulous spaces with implant-retained prostheses is funded in many countries out-of-pocket with costly implications that may limit uptake.

#### *Legal Considerations*

Not applicable.

**12.2.2 | In people with a minimum of 5 teeth missing for any reason (including stage IV periodontitis patients), does restoration of edentulous spaces improve systemic health?**

**R12.8 | Is rehabilitation of partial/full edentulism associated with better systemic health (teeth lost for any reason, including stage IV periodontitis)?**

PICOS question addressed by a SR

R12.8 - Evidence-based recommendation (1), Expert consensus-based recommendation (2)

**1. We recommend** *prosthodontically treating fully edentulous people in order to improve nutritional status.*

**2. We do not know** *if treating full edentulism is associated with improvement of frailty, cognitive function or other systemic health benefits.*

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| <b>Supporting literature</b> (Gennai et al., 2021)   |
| <b>Quality of evidence</b> Low   |
| <b>Grade of recommendation</b> Grade A – ↑↑ (1); Grade O – unclear, additional research needed (2) |
| <b>Strength of consensus</b> Unanimous consensus (0% of the group abstained due to potential Col)  |

## Background

### Intervention

People with untreated edentulism exhibit a higher prevalence of malnutrition, frailty and cognitive impairment compared to those who have been treated. Restoration of complete edentulism significantly reduces the number of patients at risk of malnutrition.

### Available evidence

#### *Number and design of included studies*

Evidence for malnutrition derives from one RCT (34 patients), one prospective cohort study (51 patients), and one cross-sectional study (343 patients) utilising the Mini Nutritional Assessment (MNA), a validated instrument covering numerous aspects of the patient's general health, nutritional state and habits. Evidence for frailty derives from a cross-sectional study (1026 patients) assessing frailty with the Groening Frailty Indicator. Cognitive Impairment was assessed in 240 patients with Mini-Mental Status Examination in a cross-sectional study.

#### *Risk of bias*

Risk of bias was evaluated through the Cochrane and Newcastle-Ottawa scale according to study design. A moderate to high risk of bias was detected. Intervention studies showed 50% of items as adequate, generating a moderate risk of bias. Observational studies were judged as moderate to high risk of bias as they reported a range of adequate items varying from 4 to 7.

#### *Effect sizes and their clinical relevance*

Treatment reduces the proportion of people at risk of malnutrition to a significant extent.

### *Consistency*

Studies are limited in number but consistent in detecting enhancement of nutritional status after rehabilitation. Levels of frailty, cognitive impairment and malnutrition are higher in untreated edentulous subjects.

### *Balance of benefit and harm*

The potential harms of any restoration are outweighed by the benefits of reducing malnutrition.

### *Overall certainty of the evidence*

Low.

### *From evidence to recommendation- additional considerations*

#### *Acceptability*

Restoration of edentulism is widely accepted and requested by patients to enhance masticatory function.

#### *Feasibility*

The restoration of edentulous spaces is widely undertaken and techniques and methods vary significantly among different countries, dental settings and healthcare systems. Overall, the vast majority of the population in many countries benefit from restoration of their edentulous spaces.

#### *Ethical Considerations*

Restoration of edentulous spaces should be advocated, especially in elderly populations, to improve masticatory function and reduce the likelihood of frailty.

#### *Economic Considerations*

Restoration of edentulous spaces incurs a wide range of costs dependent upon the type of restoration provided.

*Legal Considerations*

Not applicable.

## References

- Al-Harathi, S., Barbagallo, G., Psaila, A., d'Urso, U., & Nibali, L. (2021). Tooth loss and radiographic bone loss in patients without regular supportive care: A retrospective study. *Journal of Periodontology*. doi:10.1002/JPER.21-0415
- Al-Zahrani, M. S., Alhassani, A. A., Melis, M., & Zawawi, K. H. (2021). Depression is related to edentulism and lack of functional dentition: An analysis of NHANES data, 2005-2016. *Journal of Public Health Dentistry*, 81(3), 206-213. doi:10.1111/jphd.12433
- Allen, P. F., Thomason, J. M., Jepson, N. J., Nohl, F., Smith, D. G., & Ellis, J. (2006). A randomized controlled trial of implant-retained mandibular overdentures. *Journal of Dental Research*, 85(6), 547-551. doi:10.1177/154405910608500613
- Arn, M. L., Dritsas, K., Pandis, N., & Kloukos, D. (2020). The effects of fixed orthodontic retainers on periodontal health: A systematic review. *American Journal of Orthodontics and Dentofacial Orthopedics*, 157(2), 156-164 e117. doi:10.1016/j.ajodo.2019.10.010
- Awad, M. A., Locker, D., Korner-Bitensky, N., & Feine, J. S. (2000). Measuring the effect of intra-oral implant rehabilitation on health-related quality of life in a randomized controlled clinical trial. *Journal of Dental Research*, 79(9), 1659-1663. doi:10.1177/00220345000790090401
- Axelsson, P., & Lindhe, J. (1981). The significance of maintenance care in the treatment of periodontal disease. *Journal of Clinical Periodontology*, 8(4), 281-294. doi:10.1111/j.1600-051x.1981.tb02039.x
- Balshem, H., Helfand, M., Schunemann, H. J., Oxman, A. D., Kunz, R., Brozek, J., . . . Guyatt, G. H. (2011). GRADE guidelines: 3. Rating the quality of evidence. *Journal of Clinical Epidemiology*, 64(4), 401-406. doi:10.1016/j.jclinepi.2010.07.015
- Baumer, A., El Sayed, N., Kim, T. S., Reitmeir, P., Eickholz, P., & Pretzl, B. (2011). Patient-related risk factors for tooth loss in aggressive periodontitis after active periodontal therapy. *Journal of Clinical Periodontology*, 38(4), 347-354. doi:10.1111/j.1600-051X.2011.01698.x
- Beck, J. D., Couper, D. J., Falkner, K. L., Graham, S. P., Grossi, S. G., Gunsolley, J. C., . . . Genco, R. J. (2008). The Periodontitis and Vascular Events (PAVE) pilot study: adverse events. *Journal of Periodontology*, 79(1), 90-96. doi:10.1902/jop.2008.070223
- Bogren, A., Teles, R. P., Torresyap, G., Haffajee, A. D., Socransky, S. S., & Wennstrom, J. L. (2008). Locally delivered doxycycline during supportive periodontal therapy: a 3-year study. *Journal of Periodontology*, 79(5), 827-835. doi:10.1902/jop.2008.070515
- Brocklehurst, P. R., McKenna, G., Schimmel, M., Kossioni, A., Jerkovic-Cosic, K., Hayes, M., . . . Muller, F. (2018). How do we incorporate patient views into the design of healthcare services for older people: a discussion paper. *BMC Oral Health*, 18(1), 61. doi:10.1186/s12903-018-0513-7
- Burgett, F. G., Ramfjord, S. P., Nissle, R. R., Morrison, E. C., Charbeneau, T. D., & Caffesse, R. G. (1992). A randomized trial of occlusal adjustment in the treatment of periodontitis patients. *Journal of Clinical Periodontology*, 19(6), 381-387. doi:10.1111/j.1600-051x.1992.tb00666.x
- Buwembo, W., Munabi, I. G., Kaddumukasa, M., Kiryowa, H., Mbabali, M., Nankya, E., . . . Sewankambo, N. K. (2020). Non-surgical oral hygiene interventions on disease activity of Rheumatoid arthritis patients with periodontitis: A randomized controlled trial. *Journal of Dental Research, Dental Clinics, Dental Prospects*, 14(1), 26-36. doi:10.34172/joddd.2020.004
- Carra, M. C., Range, H., Swerts, P. J., Tuand, K., Vandamme, K., & Bouchard, P. (2021). Effectiveness of implant-supported fixed partial denture in patients with history of periodontitis: A systematic review and meta-analysis. *Journal of Clinical Periodontology*. doi:10.1111/jcpe.13481
- Caton, J. G., Armitage, G., Berglundh, T., Chapple, I. L. C., Jepsen, S., K.S., K., . . . M.S., T. (2018). A new classification scheme for periodontal and peri-implant diseases and conditions - Introduction and key



- changes from the 1999 classification. *Journal of Clinical Periodontology*, 45 (Suppl 20), S1-S8. doi:10.1111/jcpe.12935
- Chapple, I. L. C., Mealey, B. L., Van Dyke, T. E., Bartold, P. M., Dommisch, H., Eickholz, P., . . . Yoshie, H. (2018). Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of Clinical Periodontology*, 45 (Suppl 20), S68-S77. doi:10.1111/jcpe.12940
- Chapple, I. L. C., Van der Weijden, F., Doerfer, C., Herrera, D., Shapira, L., Polak, D., . . . Graziani, F. (2015). Primary prevention of periodontitis: managing gingivitis. *Journal of Clinical Periodontology*, 42 Suppl 16, S71-76. doi:10.1111/jcpe.12366
- Chen, M. X., Zhong, Y. J., Dong, Q. Q., Wong, H. M., & Wen, Y. F. (2021). Global, regional, and national burden of severe periodontitis, 1990-2019: An analysis of the Global Burden of Disease Study 2019. *Journal of Clinical Periodontology*, 48(9), 1165-1188. doi:10.1111/jcpe.13506
- Corrente, G., Abundo, R., Re, S., Cardaropoli, D., & Cardaropoli, G. (2003). Orthodontic movement into infrabony defects in patients with advanced periodontal disease: a clinical and radiological study. *Journal of Periodontology*, 74(8), 1104-1109. doi:10.1902/jop.2003.74.8.1104
- Cortellini, P., Buti, J., Pini Prato, G., & Tonetti, M. S. (2017). Periodontal regeneration compared with access flap surgery in human intra-bony defects 20-year follow-up of a randomized clinical trial: tooth retention, periodontitis recurrence and costs. *Journal of Clinical Periodontology*, 44(1), 58-66. doi:10.1111/jcpe.12638
- Cortellini, P., Stalpers, G., Mollo, A., & Tonetti, M. S. (2020). Periodontal regeneration versus extraction and dental implant or prosthetic replacement of teeth severely compromised by attachment loss to the apex: A randomized controlled clinical trial reporting 10-year outcomes, survival analysis and mean cumulative cost of recurrence. *Journal of Clinical Periodontology*, 47(6), 768-776. doi:10.1111/jcpe.13289
- Cortellini, P., Tonetti, M. S., Lang, N. P., Suvan, J. E., Zucchelli, G., Vangsted, T., . . . Adriaens, P. (2001). The simplified papilla preservation flap in the regenerative treatment of deep intrabony defects: clinical outcomes and postoperative morbidity. *Journal of Periodontology*, 72(12), 1702-1712. doi:10.1902/jop.2001.72.12.1702
- Costa, F. O., Cota, L. O. M., Cortelli, J. R., Cortelli, S. C., Cyrino, R. M., Lages, E. J. P., & Oliveira, A. P. L. (2015). Surgical and Non-Surgical Procedures Associated with Recurrence of Periodontitis in Periodontal Maintenance Therapy: 5-Year Prospective Study. *PLoS One*, 10(10), e0140847. doi:10.1371/journal.pone.0140847
- D'Aiuto, F., Orlandi, M., & Gunsolley, J. C. (2013). Evidence that periodontal treatment improves biomarkers and CVD outcomes. *Journal of Clinical Periodontology*, 40 Suppl 14, S85-105. doi:10.1111/jcpe.12061
- Dommisch, H., Walter, C., Difloe-Geisert, J. C., Gintaute, A., Jepsen, S., & Zitzmann, N. U. (2021). Efficacy of tooth splinting and occlusal adjustment in patients with periodontitis exhibiting masticatory dysfunction: A systematic review. *Journal of Clinical Periodontology*. doi:10.1111/jcpe.13563
- Donos, N., Andre Mezzomo, L., Mardas, N., Goldoni, M., & Calciolari, E. (2021). Efficacy of tooth-supported compared to implant-supported full-arch removable prostheses in patients with terminal dentition. A systematic review. *Journal of Clinical Periodontology*. doi:10.1111/jcpe.13477
- Eliasson, L. A., Hugoson, A., Kurol, J., & Siwe, H. (1982). The effects of orthodontic treatment on periodontal tissues in patients with reduced periodontal support. *European Journal of Orthodontics*, 4(1), 1-9. doi:10.1093/ejo/4.1.1
- Ericsson, I., Thilander, B., Lindhe, J., & Okamoto, H. (1977). The effect of orthodontic tilting movements on the periodontal tissues of infected and non-infected dentitions in dogs. *Journal of Clinical Periodontology*, 4(4), 278-293. doi:10.1111/j.1600-051x.1977.tb01900.x
- Fleszar, T. J., Knowles, J. W., Morrison, E. C., Burgett, F. G., Nissle, R. R., & Ramfjord, S. P. (1980). Tooth mobility and periodontal therapy. *Journal of Clinical Periodontology*, 7(6), 495-505. doi:10.1111/j.1600-051x.1980.tb02156.x

- Fu, Y. W., Li, X. X., Xu, H. Z., Gong, Y. Q., & Yang, Y. (2016). Effects of periodontal therapy on serum lipid profile and proinflammatory cytokines in patients with hyperlipidemia: a randomized controlled trial. *Clinical Oral Investigations*, 20(6), 1263-1269. doi:10.1007/s00784-015-1621-2
- G.B.D. Diseases and Injuries Collaborators. (2020). Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*, 396(10258), 1204-1222. doi:10.1016/S0140-6736(20)30925-9
- Garcia, R. I., Krall, E. A., & Vokonas, P. S. (1998). Periodontal disease and mortality from all causes in the VA Dental Longitudinal Study. *Annals of Periodontology*, 3(1), 339-349. doi:10.1902/annals.1998.3.1.339
- Gaunt, F., Devine, M., Pennington, M., Vernazza, C., Gwynnett, E., Steen, N., & Heasman, P. (2008). The cost-effectiveness of supportive periodontal care for patients with chronic periodontitis. *Journal of Clinical Periodontology*, 35(8 Suppl), 67-82. doi:10.1111/j.1600-051X.2008.01261.x
- GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. (2018). Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*, 392(10159), 1789-1858. doi:10.1016/S0140-6736(18)32279-7
- Gennai, S., Izzetti, R., Pioli, M. C., Music, L., & Graziani, F. (2021). Impact of rehabilitation versus edentulism on systemic health and quality of life in patients affected by periodontitis: A systematic review and meta-analysis. *Journal of Clinical Periodontology*. doi:10.1111/jcpe.13526
- German Association of the Scientific Medical Societies (AWMF), & Standing Guidelines Commission. (2012). AWMF Guidance Manual and Rules for Guideline Development. Retrieved from (accessed on 03.13.2020) website: <http://www.awmf.org/leitlinien/awmf-regelwerk.html>
- Gotfredsen, K., Rimborg, S., & Stavropoulos, A. (2021). Efficacy and risks of removable partial prosthesis in periodontitis patients: A systematic review. *Journal of Clinical Periodontology*. doi:10.1111/jcpe.13519
- Graetz, C., Ostermann, F., Woeste, S., Salzer, S., Dorfer, C. E., & Schwendicke, F. (2019). Long-term survival and maintenance efforts of splinted teeth in periodontitis patients. *Journal of Dentistry*, 80, 49-54. doi:10.1016/j.jdent.2018.10.009
- Griffin, S. O., Jones, J. A., Brunson, D., Griffin, P. M., & Bailey, W. D. (2012). Burden of oral disease among older adults and implications for public health priorities. *American Journal of Public Health*, 102(3), 411-418. doi:10.2105/AJPH.2011.300362
- Guyatt, G. H., Oxman, A. D., Kunz, R., Atkins, D., Brozek, J., Vist, G., . . . Schunemann, H. J. (2011). GRADE guidelines: 2. Framing the question and deciding on important outcomes. *Journal of Clinical Epidemiology*, 64(4), 395-400. doi:10.1016/j.jclinepi.2010.09.012
- Hajishengallis, G., & Chavakis, T. (2021). Local and systemic mechanisms linking periodontal disease and inflammatory comorbidities. *Nature Reviews Immunology*, 21(7), 426-440. doi:10.1038/s41577-020-00488-6
- Han, J., Dong, J., Zhao, H., Ma, Y., Yang, S., & Ma, Y. (2020). Efficacy of Periodontal Tissue Regeneration Combined with Orthodontic Therapy on Periodontitis and Its Influences on Inflammatory Factors in Patients. *Journal of Biomaterials and Tissue Engineering*, 737-742. doi:10.1166/jbt.2020.2266
- Harris, D., Hofer, S., O'Boyle, C. A., Sheridan, S., Marley, J., Benington, I. C., . . . O'Connell, B. (2013). A comparison of implant-retained mandibular overdentures and conventional dentures on quality of life in edentulous patients: a randomized, prospective, within-subject controlled clinical trial. *Clinical Oral Implants Research*, 24(1), 96-103. doi:10.1111/j.1600-0501.2011.02368.x
- Helkimo, M. (1976). Epidemiological surveys of dysfunction of the masticatory system. *Oral Sciences Reviews*, 7, 54-69.
- Herrera, D., Retamal-Valdes, B., Alonso, B., & Feres, M. (2018). Acute periodontal lesions (periodontal abscesses and necrotizing periodontal diseases) and endo-periodontal lesions. *Journal of Clinical Periodontology*, 45 Suppl 20, S78-S94. doi:10.1111/jcpe.12941

- Heydecke, G., Thomason, J. M., Lund, J. P., & Feine, J. S. (2005). The impact of conventional and implant supported prostheses on social and sexual activities in edentulous adults Results from a randomized trial 2 months after treatment. *Journal of Dentistry*, 33(8), 649-657. doi:10.1016/j.jdent.2005.01.003
- Ide, M., & Papapanou, P. N. (2013). Epidemiology of association between maternal periodontal disease and adverse pregnancy outcomes--systematic review. *Journal of Clinical Periodontology*, 40 Suppl 14, S181-194. doi:10.1111/jcpe.12063
- International Committee of Medical Editors. (2013). ICMJE Form for Disclosure of Potential Conflicts of Interest. Retrieved from <http://www.icmje.org/conflicts-of-interest/>
- Ito, K., Aida, J., Yamamoto, T., Ohtsuka, R., Nakade, M., Suzuki, K., . . . Group, J. (2015). Individual- and community-level social gradients of edentulousness. *BMC Oral Health*, 15, 34. doi:10.1186/s12903-015-0020-z
- Jeffcoat, M. K., Geurs, N. C., Reddy, M. S., Goldenberg, R. L., & Hauth, J. C. (2001). Current evidence regarding periodontal disease as a risk factor in preterm birth. *Annals of Periodontology*, 6(1), 183-188. doi:10.1902/annals.2001.6.1.183
- Jenkins, W. M., Said, S. H., Radvar, M., & Kinane, D. F. (2000). Effect of subgingival scaling during supportive therapy. *Journal of Clinical Periodontology*, 27(8), 590-596.
- Jepsen, K., Tietmann, C., Kutschera, E., Wullenweber, P., Jager, A., Cardaropoli, D., . . . Jepsen, S. (2021). The effect of timing of orthodontic therapy on the outcomes of regenerative periodontal surgery in patients with stage IV periodontitis: A multicenter randomized trial. *Journal of Clinical Periodontology*, 48(10), 1282-1292. doi:10.1111/jcpe.13528
- Jepsen, S., Caton, J. G., Albandar, J. M., Bissada, N. F., Bouchard, P., Cortellini, P., . . . Yamazaki, K. (2018). Periodontal manifestations of systemic diseases and developmental and acquired conditions: Consensus report of workgroup 3 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of Clinical Periodontology*, 45(Suppl 20), S219-S229. doi:10.1111/jcpe.12951
- Jiang, C., Fan, C., Yu, X., Xu, T., Cai, J., Fan, X., & Zhang, J. (2021). Comparison of the efficacy of different periodic periodontal scaling protocols for oral hygiene in adolescents with fixed orthodontic appliances: A prospective cohort study. *American Journal of Orthodontics and Dentofacial Orthopedics*, 159(4), 435-442. doi:10.1016/j.ajodo.2020.01.026
- Kaldahl, W. B., Kalkwarf, K. L., Patil, K. D., Molvar, M. P., & Dyer, J. K. (1996a). Long-term evaluation of periodontal therapy: I. Response to 4 therapeutic modalities. *Journal of Periodontology*, 67(2), 93-102. doi:10.1902/jop.1996.67.2.93
- Kaldahl, W. B., Kalkwarf, K. L., Patil, K. D., Molvar, M. P., & Dyer, J. K. (1996b). Long-term evaluation of periodontal therapy: II. Incidence of sites breaking down. *Journal of Periodontology*, 67(2), 103-108. doi:10.1902/jop.1996.67.2.103
- Kassebaum, N. J., Bernabe, E., Dahiya, M., Bhandari, B., Murray, C. J., & Marcenes, W. (2014). Global Burden of Severe Tooth Loss: A Systematic Review and Meta-analysis. *Journal of Dental Research*, 93(7 Suppl), 20S-28S. doi:10.1177/0022034514537828
- Kayser, A. F. (1981). Shortened dental arches and oral function. *Journal of Oral Rehabilitation*, 8(5), 457-462. doi:10.1111/j.1365-2842.1981.tb00519.x
- Kerry, G. J., Morrison, E. C., Ramfjord, S. P., Hill, R. W., Caffesse, R. G., Nissle, R. R., & Appleberry, E. A. (1982). Effect of periodontal treatment on tooth mobility. *Journal of Periodontology*, 53(10), 635-638. doi:10.1902/jop.1982.53.10.635
- Kloukos, D., Rocuzzo, A., Stahli, A., Sculean, A., Katsaros, C., & Salvi, G. E. (2021). Effect of combined periodontal and orthodontic treatment of tilted molars and of teeth with intra-bony and furcation defects in stage-IV periodontitis patients: A systematic review. *Journal of Clinical Periodontology*. doi:10.1111/jcpe.13509

- Kraal, J. H., Digiancinto, J. J., Dail, R. A., Lemmerman, K., & Peden, J. W. (1980). Periodontal conditions in patients after molar uprighting. *Journal of Prosthetic Dentistry*, *43*(2), 156-162. doi:10.1016/0022-3913(80)90179-1
- Kwok, V., & Caton, J. G. (2007). Commentary: prognosis revisited: a system for assigning periodontal prognosis. *Journal of Periodontology*, *78*(11), 2063-2071. doi:10.1902/jop.2007.070210
- Lang, N. P., Suvan, J. E., & Tonetti, M. S. (2015). Risk factor assessment tools for the prevention of periodontitis progression a systematic review. *Journal of Clinical Periodontology*, *42 Suppl 16*, S59-70. doi:10.1111/jcpe.12350
- Lang, N. P., & Tonetti, M. S. (1996). Periodontal diagnosis in treated periodontitis. Why, when and how to use clinical parameters. *Journal of Clinical Periodontology*, *23*(3 Pt 2), 240-250. doi:10.1111/j.1600-051x.1996.tb02083.x
- Lang, N. P., & Tonetti, M. S. (2003). Periodontal risk assessment (PRA) for patients in supportive periodontal therapy (SPT). *Oral Health & Preventive Dentistry*, *1*(1), 7-16.
- Laudisio, A., Gemma, A., Fontana, D. O., Rivera, C., Bandinelli, S., Ferrucci, L., & Incalzi, R. A. (2016). Self-Reported Masticatory Dysfunction and Mortality in Community Dwelling Elderly Adults: A 9-Year Follow-Up. *Journal of the American Geriatrics Society*, *64*(12), 2503-2510. doi:10.1111/jgs.14331
- Leow, N. M., Moreno, F., Marletta, D., Hussain, S. B., Buti, J., Almond, N., & Needleman, I. (2021). Recurrence and progression of periodontitis and methods of management in long-term care: A systematic review and meta-analysis. *Journal of Clinical Periodontology*. doi:10.1111/jcpe.13553
- Linden, G. J., Linden, K., Yarnell, J., Evans, A., Kee, F., & Patterson, C. C. (2012). All-cause mortality and periodontitis in 60-70-year-old men: a prospective cohort study. *Journal of Clinical Periodontology*, *39*(10), 940-946. doi:10.1111/j.1600-051X.2012.01923.x
- Lindhe, J., Meyle, J., & Group, D. o. E. W. o. P. (2008). Peri-implant diseases: Consensus Report of the Sixth European Workshop on Periodontology. *Journal of Clinical Periodontology*, *35*(8 Suppl), 282-285. doi:10.1111/j.1600-051X.2008.01283.x
- Littlewood, S. J., Millett, D. T., Doubleday, B., Bearn, D. R., & Worthington, H. V. (2016). Retention procedures for stabilising tooth position after treatment with orthodontic braces. *Cochrane Database of Systematic Reviews*(1), CD002283. doi:10.1002/14651858.CD002283.pub4
- Loos, B. G., & Needleman, I. (2020). Endpoints of active periodontal therapy. *Journal of Clinical Periodontology*, *47*, 61-71. doi:10.1111/jcpe.13253
- Machtei, E. E., Norderyd, J., Koch, G., Dunford, R., Grossi, S., & Genco, R. J. (1993). The rate of periodontal attachment loss in subjects with established periodontitis. *Journal of Periodontology*, *64*(8), 713-718. doi:10.1902/jop.1993.64.8.713
- Marcenes, W., Kassebaum, N. J., Bernabe, E., Flaxman, A., Naghavi, M., Lopez, A., & Murray, C. J. (2013). Global burden of oral conditions in 1990-2010: a systematic analysis. *Journal of Dental Research*, *92*(7), 592-597. doi:10.1177/0022034513490168
- Martín, C., Celis, B., Ambrosio, N., Bollain, J., Antonoglou, G. N., & Figuero, E. (2021). Effect of orthodontic therapy in periodontitis and non-periodontitis patients: a systematic review with meta-analysis. *Journal of Clinical Periodontology*. doi:10.1111/jcpe.13487
- Martin, J. A., Page, R. C., Kaye, E. K., Hamed, M. T., & Loeb, C. F. (2009). Periodontitis severity plus risk as a tooth loss predictor. *Journal of Periodontology*, *80*(2), 202-209. doi:10.1902/jop.2009.080363
- Martin, J. A., Page, R. C., Loeb, C. F., & Levi, P. A. J. (2010). Tooth loss in 776 treated periodontal patients. *Journal of Periodontology*, *81*(2), 244-250. doi:<https://dx.doi.org/10.1902/jop.2009.090184>
- Matuliene, G., Pjetursson, B. E., Salvi, G. E., Schmidlin, K., Bragger, U., Zwahlen, M., & Lang, N. P. (2008). Influence of residual pockets on progression of periodontitis and tooth loss: results after 11 years of maintenance. *Journal of Clinical Periodontology*, *35*(8), 685-695. doi:CPE1245 [pii]10.1111/j.1600-051X.2008.01245.x

- McGuire, M. K., & Nunn, M. E. (1996). Prognosis versus actual outcome. II. The effectiveness of clinical parameters in developing an accurate prognosis. *Journal of Periodontology*, 67(7), 658-665. doi:10.1902/jop.1996.67.7.658
- Melsen, B. (1986). Tissue reaction following application of extrusive and intrusive forces to teeth in adult monkeys. *American Journal of Orthodontics*, 89(6), 469-475. doi:10.1016/0002-9416(86)90002-3
- Melsen, B., Agerbaek, N., & Markenstam, G. (1989). Intrusion of incisors in adult patients with marginal bone loss. *American Journal of Orthodontics and Dentofacial Orthopedics*, 96(3), 232-241. doi:10.1016/0889-5406(89)90460-5
- Meyle, J., & Chapple, I. (2015). Molecular aspects of the pathogenesis of periodontitis. *Periodontology 2000*, 69(1), 7-17. doi:10.1111/prd.12104
- Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Journal of Clinical Epidemiology*, 62(10), 1006-1012. doi:10.1016/j.jclinepi.2009.06.005
- Montero, E., Lopez, M., Vidal, H., Martinez, M., Virto, L., Marrero, J., . . . Sanz, M. (2020). Impact of periodontal therapy on systemic markers of inflammation in patients with metabolic syndrome: A randomized clinical trial. *Diabetes, Obesity and Metabolism*, 22(11), 2120-2132. doi:10.1111/dom.14131
- Montero, E., Molina, A., Palombo, D., Moron, B., Pradies, G., & Sanz-Sanchez, I. (2021). Efficacy and risks of tooth-supported prostheses in the treatment of partially edentulous patients with stage IV periodontitis. A systematic review and meta-analysis. *Journal of Clinical Periodontology*. doi:10.1111/jcpe.13482
- Muller, F., Duvernay, E., Loup, A., Vazquez, L., Herrmann, F. R., & Schimmel, M. (2013). Implant-supported mandibular overdentures in very old adults: a randomized controlled trial. *Journal of Dental Research*, 92(12 Suppl), 154S-160S. doi:10.1177/0022034513509630
- Murphy, M. K., Black, N. A., Lamping, D. L., McKee, C. M., Sanderson, C. F., Askham, J., & Marteau, T. (1998). Consensus development methods, and their use in clinical guideline development. *Health Technology Assessment*, 2(3), i-iv, 1-88.
- Nguyen, V. B., Nguyen, T. T., Huynh, N. C., Nguyen, K. D., Le, T. A., & Hoang, H. T. (2021). Effects of non-surgical periodontal treatment in rheumatoid arthritis patients: A randomized clinical trial. *Dental and Medical Problems*, 58(1), 97-105. doi:10.17219/dmp/131266
- Nyman, S. R., & Lang, N. P. (1994). Tooth mobility and the biological rationale for splinting teeth. *Periodontology 2000*, 4, 15-22. doi:10.1111/j.1600-0757.1994.tb00002.x
- Offenbacher, S., Katz, V., Fertik, G., Collins, J., Boyd, D., Maynor, G., . . . Beck, J. (1996). Periodontal infection as a possible risk factor for preterm low birth weight. *Journal of Periodontology*, 67(10 Suppl), 1103-1113. doi:10.1902/jop.1996.67.10s.1103
- Orlandi, M., Munoz Aguilera, E., Marletta, D., Petrie, A., Suvan, J., & D'Aiuto, F. (2021). Impact of the treatment of periodontitis on systemic health and quality of life: A systematic review. *Journal of Clinical Periodontology*. doi:10.1111/jcpe.13554
- Page, R. C., Martin, J., Krall, E. A., Mancl, L., & Garcia, R. (2003). Longitudinal validation of a risk calculator for periodontal disease. *Journal of Clinical Periodontology*, 30(9), 819-827. doi:10.1034/j.1600-051x.2003.00370.x
- Papageorgiou, S. N., Antonoglou, G. N., Michelogiannakis, D., Kakali, L., Eliades, T., & Madianos, P. (2021). Effect of periodontal-orthodontic treatment of teeth with pathological tooth flaring, drifting and elongation in patients with severe periodontitis: a systematic review with meta-analysis. *Journal of Clinical Periodontology*. doi:10.1111/jcpe.13529
- Papapanou, P. N., Sanz, M., Buduneli, N., Dietrich, T., Feres, M., Fine, D. H., . . . Tonetti, M. S. (2018). Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of Clinical Periodontology*, 45(Suppl 20), S162-S170. doi:10.1111/jcpe.12946

- Parker, M. L., Thornton-Evans, G., Wei, L., & Griffin, S. O. (2020). Prevalence of and Changes in Tooth Loss Among Adults Aged  $\geq 50$  Years with Selected Chronic Conditions - United States, 1999-2004 and 2011-2016. *Morbidity and Mortality Weekly Report*, *69*(21), 641-646. doi:10.15585/mmwr.mm6921a1
- Pennington, M., Heasman, P., Gaunt, F., Guntsch, A., Ivanovski, S., Imazato, S., . . . Vernazza, C. (2011). The cost-effectiveness of supportive periodontal care: a global perspective. *Journal of Clinical Periodontology*, *38*(6), 553-561. doi:10.1111/j.1600-051X.2011.01722.x
- Qureshi, A., Bokhari, S. A. H., Haque, Z., Baloch, A. A., & Zaheer, S. (2021). Clinical efficacy of scaling and root planing with and without metronidazole on glycemic control: three-arm randomized controlled trial. *BMC Oral Health*, *21*(1), 253. doi:10.1186/s12903-021-01620-1
- Ramanauskaitė, A., Becker, K., Wolfart, S., Lukman, F., & Schwarz, F. (2021). Efficacy of rehabilitation with different approaches of implant-supported full-arch prosthetic designs: A systematic review. *Journal of Clinical Periodontology*. doi:10.1111/jcpe.13540
- Ramseier, C. A., Anerud, A., Dulac, M., Lulic, M., Cullinan, M. P., Seymour, G. J., . . . Lang, N. P. (2017). Natural history of periodontitis: Disease progression and tooth loss over 40 years. *Journal of Clinical Periodontology*, *44*(12), 1182-1191. doi:10.1111/jcpe.12782
- Ramseier, C. A., Nydegger, M., Walter, C., Fischer, G., Sculean, A., Lang, N. P., & Salvi, G. E. (2019). Time between recall visits and residual probing depths predict long-term stability in patients enrolled in supportive periodontal therapy. *Journal of Clinical Periodontology*, *46*(2), 218-230. doi:10.1111/jcpe.13041.
- Ramseier, C. A., Woelber, J. P., Kitzmann, J., Detzen, L., Carra, M. C., & Bouchard, P. (2020). Impact of risk factor control interventions for smoking cessation and promotion of healthy lifestyles in patients with periodontitis: a systematic review. *Journal of Clinical Periodontology*, *47*(S22), 90-106. doi:10.1111/jcpe.13240
- Rapone, B., Ferrara, E., Corsalini, M., Qorri, E., Converti, I., Lorusso, F., . . . Scarano, A. (2021). Inflammatory Status and Glycemic Control Level of Patients with Type 2 Diabetes and Periodontitis: A Randomized Clinical Trial. *International Journal of Environmental Research and Public Health*, *18*(6). doi:10.3390/ijerph18063018
- Ravida, A., Qazi, M., Troiano, G., Saleh, M. H. A., Greenwell, H., Kornman, K., & Wang, H. L. (2020). Using periodontal staging and grading system as a prognostic factor for future tooth loss: A long-term retrospective study. *Journal of Periodontology*, *91*(4), 454-461. doi:10.1002/JPER.19-0390
- Ravida, A., Travan, S., Saleh, M. H. A., Greenwell, H., Papapanou, P. N., Sanz, M., . . . Kornman, K. (2021). Agreement among international periodontal experts using the 2017 World Workshop classification of periodontitis. *Journal of Periodontology*. doi:10.1002/JPER.20-0825
- Righolt, A. J., Jevdjevic, M., Marcenes, W., & Listl, S. (2018). Global-, Regional-, and Country-Level Economic Impacts of Dental Diseases in 2015. *Journal of Dental Research*, *97*(5), 501-507. doi:10.1177/0022034517750572
- Rosling, B., Serino, G., Hellstrom, M. K., Socransky, S. S., & Lindhe, J. (2001). Longitudinal periodontal tissue alterations during supportive therapy. Findings from subjects with normal and high susceptibility to periodontal disease. *Journal of Clinical Periodontology*, *28*(3), 241-249. doi:10.1034/j.1600-051x.2001.028003241.x
- Saleh, M. H. A., Dukka, H., Troiano, G., Ravida, A., Qazi, M., Wang, H. L., & Greenwell, H. (2021). Long term comparison of the prognostic performance of PerioRisk, periodontal risk assessment, periodontal risk calculator, and staging and grading systems. *Journal of Periodontology*. doi:10.1002/JPER.20-0662
- Salonen, L., Hellden, L., & Carlsson, G. E. (1990). Prevalence of signs and symptoms of dysfunction in the masticatory system: an epidemiologic study in an adult Swedish population. *Journal of Craniomandibular Disorders*, *4*(4), 241-250.
- Saminsky, M., Halperin-Sternfeld, M., Machtei, E. E., & Horwitz, J. (2015). Variables affecting tooth survival and changes in probing depth: a long-term follow-up of periodontitis patients. *Journal of Clinical Periodontology*, *42*(6), 513-519. doi:10.1111/jcpe.12419

- Sanz, M., Ceriello, A., Buyschaert, M., Chapple, I., Demmer, R. T., Graziani, F., . . . Vegh, D. (2018). Scientific evidence on the links between periodontal diseases and diabetes: Consensus report and guidelines of the joint workshop on periodontal diseases and diabetes by the International Diabetes Federation and the European Federation of Periodontology. *Journal of Clinical Periodontology*, *45*(2), 138-149. doi:10.1111/jcpe.12808
- Sanz, M., Herrera, D., Kebschull, M., Chapple, I., Jepsen, S., Berglundh, T., . . . EFP workshop participants methodological consultants. (2020). Treatment of Stage I-III Periodontitis -The EFP S3 Level Clinical Practice Guideline. *Journal of Clinical Periodontology*, *47*, 4-60. doi:10.1111/jcpe.13290
- Sanz, M., Kornman, K., & Working group 3 of joint EFP/AAP Workshop. (2013). Periodontitis and adverse pregnancy outcomes: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *Journal of Clinical Periodontology*, *40 Suppl 14*, S164-169. doi:10.1111/jcpe.12083
- Sanz, M., Marco Del Castillo, A., Jepsen, S., Gonzalez-Juanatey, J. R., D'Aiuto, F., Bouchard, P., . . . Wimmer, G. (2020). Periodontitis and cardiovascular diseases: Consensus report. *Journal of Clinical Periodontology*, *47*(3), 268-288. doi:10.1111/jcpe.13189
- Sanz, M., Papapanou, P. N., Tonetti, M. S., Greenwell, H., & Kornman, K. (2020). Guest Editorial: Clarifications on the use of the new classification of periodontitis. *Journal of Clinical Periodontology*, *47*(6), 658-659. doi:10.1111/jcpe.13286
- Sato, M., Iwasaki, M., Yoshihara, A., & Miyazaki, H. (2016). Association between periodontitis and medical expenditure in older adults: A 33-month follow-up study. *Geriatrics and Gerontology International*, *16*(7), 856-864. doi:10.1111/ggi.12569
- Schunemann, H. J., Al-Ansary, L. A., Forland, F., Kersten, S., Komulainen, J., Kopp, I. B., . . . Board of Trustees of the Guidelines International Network. (2015). Guidelines International Network: Principles for Disclosure of Interests and Management of Conflicts in Guidelines. *Annals of Internal Medicine*, *163*(7), 548-553. doi:10.7326/M14-1885
- Schunemann, H. J., Wiercioch, W., Brozek, J., Etzeandia-Ikobaltzeta, I., Mustafa, R. A., Manja, V., . . . Akl, E. A. (2017). GRADE Evidence to Decision (EtD) frameworks for adoption, adaptation, and de novo development of trustworthy recommendations: GRADE-ADOLOPMENT. *Journal of Clinical Epidemiology*, *81*, 101-110. doi:10.1016/j.jclinepi.2016.09.009
- Schunemann, H. J., Zhang, Y., Oxman, A. D., & Expert Evidence in Guidelines, G. (2019). Distinguishing opinion from evidence in guidelines. *British Medical Journal*, *366*, l4606. doi:10.1136/bmj.l4606
- Schwarz, F., Derks, J., Monje, A., & Wang, H. L. (2018). Peri-implantitis. *Journal of Clinical Periodontology*, *45 Suppl 20*, S246-S266. doi:10.1111/jcpe.12954
- Shanbhag, S., Dahiya, M., & Croucher, R. (2012). The impact of periodontal therapy on oral health-related quality of life in adults: a systematic review. *Journal of Clinical Periodontology*, *39*(8), 725-735. doi:10.1111/j.1600-051X.2012.01910.x
- Sharma, P., Dietrich, T., Ferro, C. J., Cockwell, P., & Chapple, I. L. (2016). Association between periodontitis and mortality in stages 3-5 chronic kidney disease: NHANES III and linked mortality study. *Journal of Clinical Periodontology*, *43*(2), 104-113. doi:10.1111/jcpe.12502
- Shea, B. J., Reeves, B. C., Wells, G., Thuku, M., Hamel, C., Moran, J., . . . Henry, D. A. (2017). AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *British Medical Journal*, *358*, j4008. doi:10.1136/bmj.j4008
- Simpson, T. C., Weldon, J. C., Worthington, H. V., Needleman, I., Wild, S. H., Moles, D. R., . . . Iheozor-Ejiofor, Z. (2015). Treatment of periodontal disease for glycaemic control in people with diabetes mellitus. *Cochrane Database of Systematic Reviews*(11), CD004714. doi:10.1002/14651858.CD004714.pub3
- Soder, B., Jin, L. J., Klinge, B., & Soder, P. O. (2007). Periodontitis and premature death: a 16-year longitudinal study in a Swedish urban population. *Journal of Periodontal Research*, *42*(4), 361-366. doi:10.1111/j.1600-0765.2006.00957.x

- Soikkonen, K., Wolf, J., Salo, T., & Tilvis, R. (2000). Radiographic periodontal attachment loss as an indicator of death risk in the elderly. *Journal of Clinical Periodontology*, 27(2), 87-92. doi:10.1034/j.1600-051x.2000.027002087.x
- Sonnenschein, S. K., Betzler, C., Rutters, M. A., Krisam, J., Saure, D., & Kim, T. S. (2017). Long-term stability of splinted anterior mandibular teeth during supportive periodontal therapy. *Acta Odontologica Scandinavica*, 75(7), 475-482. doi:10.1080/00016357.2017.1340668
- Sonnenschein, S. K., Ciardo, A., Kilian, S., Ziegler, P., Ruetters, M., Splindler, M., & Kim, T. S. (2021). The impact of splinting timepoint of mobile mandibular incisors on the outcome of periodontal treatment-preliminary observations from a randomized clinical trial. *Clinical Oral Investigations*. doi:10.1007/s00784-021-04075-4
- Sonnenschein, S. K., Ziegler, P., Ciardo, A., Ruetters, M., Krisam, J., & Kim, T. S. (2021). The impact of splinting mobile mandibular incisors on Oral Health-Related Quality of Life-Preliminary observations from a randomized clinical trial. *Journal of Clinical Periodontology*, 48(6), 816-825. doi:10.1111/jcpe.13454
- The Economist Intelligence Unit. (2021). *Time to take gum disease seriously: The societal and economic impact of periodontitis*. Retrieved from <https://eiuPerspectives.economist.com/healthcare/time-take-gum-disease-seriously-societal-and-economic-impact-periodontitis>
- Tietmann, C., Broseler, F., Axelrad, T., Jepsen, K., & Jepsen, S. (2021). Regenerative periodontal surgery and orthodontic tooth movement in stage IV periodontitis: A retrospective practice-based cohort study. *Journal of Clinical Periodontology*, 48(5), 668-678. doi:10.1111/jcpe.13442
- Tomasi, C., Albouy, J. P., Schaller, D., Navarro, R. C., & Derks, J. (2021). Efficacy of rehabilitation of stage IV periodontitis patients with full-arch fixed prostheses: Tooth-supported versus Implant-supported-A systematic review. *Journal of Clinical Periodontology*. doi:10.1111/jcpe.13511
- Tonetti, M. S., D'Aiuto, F., Nibali, L., Donald, A., Storry, C., Parkar, M., . . . Deanfield, J. (2007). Treatment of periodontitis and endothelial function. *New England Journal of Medicine*, 356(9), 911-920. doi:10.1056/NEJMoa063186
- Tonetti, M. S., Greenwell, H., & Kornman, K. S. (2018). Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. *Journal of Clinical Periodontology*, 45 Suppl 20, S149-S161. doi:10.1111/jcpe.12945
- Tonetti, M. S., Jepsen, S., Jin, L., & Otomo-Corgel, J. (2017). Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: A call for global action. *Journal of Clinical Periodontology*, 44(5), 456-462. doi:10.1111/jcpe.12732
- Tonetti, M. S., Lang, N. P., Cortellini, P., Suvan, J. E., Eickholz, P., Fourmoussis, I., . . . Wallkamm, B. (2012). Effects of a single topical doxycycline administration adjunctive to mechanical debridement in patients with persistent/recurrent periodontitis but acceptable oral hygiene during supportive periodontal therapy. *Journal of Clinical Periodontology*, 39(5), 475-482. doi:10.1111/j.1600-051X.2012.01864.x
- Tonetti, M. S., & Sanz, M. (2019). Implementation of the new classification of periodontal diseases: Decision-making algorithms for clinical practice and education. *Journal of Clinical Periodontology*, 46(4), 398-405. doi:10.1111/jcpe.13104
- Tonetti, M. S., Van Dyke, T. E., & Working group 1 of the joint EFP/AAP Workshop. (2013). Periodontitis and atherosclerotic cardiovascular disease: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *Journal of Clinical Periodontology*, 40 Suppl 14, S24-29. doi:10.1111/jcpe.12089
- Trombelli, L., Franceschetti, G., & Farina, R. (2015). Effect of professional mechanical plaque removal performed on a long-term, routine basis in the secondary prevention of periodontitis: a systematic review. *Journal of Clinical Periodontology*, 42 Suppl 16, S221-236. doi:10.1111/jcpe.12339
- Trombelli, L., Minenna, L., Toselli, L., Zaetta, A., Checchi, L., Checchi, V., . . . Farina, R. (2017). Prognostic value of a simplified method for periodontal risk assessment during supportive periodontal therapy. *Journal of Clinical Periodontology*, 44(1), 51-57. doi:10.1111/jcpe.12645



- Trombelli, L., Simonelli, A., Franceschetti, G., Maietti, E., & Farina, R. (2020). What periodontal recall interval is supported by evidence? *Periodontology 2000*, *84*(1), 124-133. doi:10.1111/prd.12340
- Tsakos, G., Allen, P. F., Steele, J. G., & Locker, D. (2012). Interpreting oral health-related quality of life data. *Community Dentistry and Oral Epidemiology*, *40*(3), 193-200. doi:10.1111/j.1600-0528.2011.00651.x
- Uy, S., Deng, K., Fok, C. T. C., Fok, M. R., Pelekos, G., & Tonetti, M. S. (2021). Food Intake, Masticatory Function, Tooth Mobility, Loss of Posterior Support and Diminished Quality of Life Are Associated with More Advanced Periodontitis Stage Diagnosis. *Journal of Clinical Periodontology*. doi:10.1111/jcpe.13588
- Walter, M. H., Dreyhaupt, J., Hannak, W., Wolfart, S., Luthardt, R. G., Stark, H., . . . Heydecke, G. (2018). The Randomized Shortened Dental Arch Study: Tooth Loss Over 10 Years. *International Journal of Prosthodontics*, *31*(1), 77-84. doi:10.11607/ijp.5368
- Walter, M. H., Dreyhaupt, J., Mundt, T., Kohal, R., Kern, M., Rauch, A., . . . Marre, B. (2020). Periodontal health in shortened dental arches: A 10-year RCT. *Journal of Prosthodontic Research*, *64*(4), 498-505. doi:10.1016/j.jpor.2020.01.005
- Wennstrom, J. L., Stokland, B. L., Nyman, S., & Thilander, B. (1993). Periodontal tissue response to orthodontic movement of teeth with infrabony pockets. *American Journal of Orthodontics and Dentofacial Orthopedics*, *103*(4), 313-319. doi:10.1016/0889-5406(93)70011-C
- Zhou, Q. B., Xia, W. H., Ren, J., Yu, B. B., Tong, X. Z., Chen, Y. B., . . . Yang, J. Y. (2017). Effect of Intensive Periodontal Therapy on Blood Pressure and Endothelial Microparticles in Patients With Prehypertension and Periodontitis: A Randomized Controlled Trial. *Journal of Periodontology*, *88*(8), 711-722. doi:10.1902/jop.2017.160447
- Zitzmann, N. U., Rohner, U., Weiger, R., & Krastl, G. (2009). When to choose which retention element to use for removable dental prostheses. *International Journal of Prosthodontics*, *22*(2), 161-167.