INSTITUTO UNIVERSITÁRIO EGAS MONIZ

MESTRADO INTEGRADO EM MEDICINA DENTÁRIA

GLOBAL PREVALENCE OF PERIODONTITIS BETWEEN 2011 AND 2020: A SYSTEMATIC REVIEW AND META-ANALYSIS

Trabalho submetido por
Diogo António Monteiro Trindade
para a obtenção do grau de Mestre em Medicina Dentária

setembro de 2022

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Trabalho orientado por
Prof. Doutor José João Mendes

e coorientado por
Prof. Doutor João Botelho e Prof. Doutor Leandro Chambrone

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Abstract

Background: Periodontitis is a chronic inflammatory disease, and its high prevalence contributes to the burden of chronic diseases, representing a public health problem. This systematic review aimed to estimate the pooled prevalence of periodontitis between 2011 and 2020.

Material & Methods: Electronic search in PUBMED, Web of Science and LILACS focused on epidemiological studies reporting the prevalence of periodontitis conducted between 2011 and 2020 for inclusion. We grouped studies according to the periodontal case definition and conducted random effects meta-analyses with double arcsine transformation. We explored the effect of confounding variables to the overall estimates using subgroup and meta-regression analyses.

Results: A total of 83 papers regarding 81 studies were included. The results displayed a significant difference with confident case definitions (62.5%) reporting nearly twice the prevalence than non-confident classifications (37.0%). Estimates using confident periodontal case definitions showed a pooled prevalence of periodontitis of 62.5%, comprising 18 different countries. Estimates reporting using Centers for Disease Control/American Academy of Periodontology (CDC/AAP) (2012) case definition presented the highest estimate (68.0%) and the CDC/AAP (2007) presented the lowest (49.1%). Age was a relevant confounding variable as older participants (≥65 years old) had the highest pooled estimate (79.4%).

Conclusions: Between 2011 and 2020, periodontitis was estimated to be around 63%, and severe periodontitis to be at 24.2%.

Keywords: Periodontal Disease; Periodontitis; Systematic Review; Prevalence.

Resumo

Contexto: A periodontite constitui uma doença inflamatória crónica e contribui para a carga de doenças crónicas, devido à sua elevada prevalência mundial, representando um problema de saúde pública. Esta revisão sistemática visou avaliar a estimativa de prevalência de periodontite entre 2011 e 2020.

Materiais e Métodos: Foi realizada uma pesquisa nas bases de dados PUBMED, Web of Science e LILACS focando-se na inclusão de estudos epidemiológicos referentes à prevalência de periodontite realizados entre 2011 e 2020. Agrupámos os estudos de acordo com a classificação de periodontite e efetuámos meta-análises de efeitos aleatórios com transformação dupla arcsina. Análises de subgrupo de sensibilidade e meta-regressão avaliaram o efeito de variáveis de confusão para as estimativas gerais.

Resultados: 81 artigos relativos a 80 estudos foram incluídos. Os resultados confirmaram uma diferença significativa das classificações confiáveis (62.5%), quase o dobro da prevalência que as classificações não confiáveis (37,0%). Estimativas usando definições confiáveis mostraram uma prevalência combinada de periodontite de 62,5%, abrangendo 18 países. Estimativas relatadas usando a definição do Centers for Disease Control/American Academy of Periodontology (CDC/AAP) (2012) apresentaram a maior estimativa (68,0%) e o CDC/AAP (2007) a menor (49,1%). A idade foi uma variável de confusão relevante, dado que pacientes mais velhos (≥65 anos) apresentaram a maior estimativa combinada (79,4%).

Conclusões: Entre 2011 e 2020, a periodontite foi estimada em cerca de 63% e a periodontite severa em 24,2%.

Palavras-chave: Doença Periodontal; Periodontite; Revisão Sistemática; Prevalência.

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List of Abbreviation

AAP – American Academy of Periodontology

CAL – Clinical Attachment Loss

CI – Confidence Interval

CDC – Centers for Disease Control

CPI – Community Periodontal Index

DM – Diabetes Mellitus

EFP – European Federation of Periodontology

ES – Effect Size

FRP – Full-mouth Recording Protocol

ICAMs – Intercellular Adhesion Molecules

IL- 8 – Interleukin- 8

LILACS – *Literatura Latino-Americana e do Caribe em Ciências da Saúde*

MEDLINE – Medical Literature Analysis and Retrieval System Online

MeShs – Medical Subject Headings

NR – Not Reported

OHRQoL – Oral Health Related Quality of Life

OPG – Osteoprotegerin

PPD – Periodontal Probing Depth

PP – Pooled Prevalence

PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PRP – Partial-mouth Recording Protocol

RANKL – Receptor Activator of Nuclear Factor k Ligand

SP – Severe Periodontitis

USA – United States of America

WHO – World Health Organization

I. INTRODUCTION

1. PERIODONTITIS

Periodontal diseases is a group of diseases affecting the periodontium (the surrounding and supporting structures of the tooth), and can be divided into gingivitis and periodontitis (Armitage, 1999; Caton et al., 2018; Tonetti et al., 2018). In detail, periodontitis is a chronic inflammatory disease induced by the disruption of the balance between the host defense and the subgingival microflora, leading to the detachment of connective tissue, loss of alveolar bone, and formation of pathological periodontal pockets (E. Lee & Lee, 2019).

If left untreated, tooth loss may be an inevitable outcome of periodontitis, reducing the oral health-related quality of life (OHRQoL) (Fischer et al., 2020; Helmi et al., 2019; Sun et al., 2020). Periodontitis poses a serious public health issue and has a substantial socioeconomic effect., being responsible, in 2018, for a total cost of approximately $154.06B across the United States of America (USA), and €158.64B in Europe (Botelho et al., 2019, 2021).

From 1990 to 2010, the Global Burden of Disease rated severe periodontitis as the sixth most prevalent disease worldwide, with an 11% prevalence, about 743 million adults (Kassebaum et al., 2014; Marcenes et al., 2013). Additionally, from 2009 to 2010, 30% of the population in the USA had moderate periodontitis (Eke, Dye, et al., 2012), while in Portugal, it was estimated a prevalence of around 60% in the Southern region of the Lisbon Metropolitan Area (Botelho et al., 2019).

From the abovementioned data, the access to the current trends of periodontitis allows for better understanding of the relatively maintained high prevalence of periodontitis. Thus, this bulk of information contributes to a better planning of dental services and workforce, providing a distinctive perspective for developing public health policies (Kassebaum et al., 2017).

1.1. Clinical Manifestations

During tooth emergence, the junctional epithelium starts to cover the surface of the tooth, and a region known as the gingival sulcus is created in the middle of the enamel and the oral epithelium, which is lined by the sulcular epithelium and contains gingival crevicular fluid (Nibali, 2018). This fluid, which is regarded as an osmotic capillary transudate in terms of gingival health, is constituted by various components, namely: oral bacteria, leukocytes, antibodies, cytokines, enzymes, and products of tissue breakdown (Donos, 2018). The junctional epithelium exhibits subclinical symptoms of inflammation in a physiologically sound state (Nibali, 2018).

A diverse community of microorganisms, known as dental plaque, can be found on the tooth surface, normally at stagnant sites protected from toothbrushing forces (Marsh, 2004). The resident plaque microflora is comparatively stable after the initial establishment, however, if the composition varies, different bacteria established in the subgingival plaque may lead to a disruption of the physiological state (Hajishengallis, 2015). Upon disturbance of the periodontium homeostasis, the gingival inflammation increases, along with the change of the transudate from the gingival crevicular fluid to an inflammatory exudate. Moreover, deepening of the gingival sulcus occurs, as well as formation of pathological periodontal pocket with the conversion of junctional epithelium into ‘pocket epithelium’ (Ebersole, 2003; Nibali, 2018) (Figure 1).

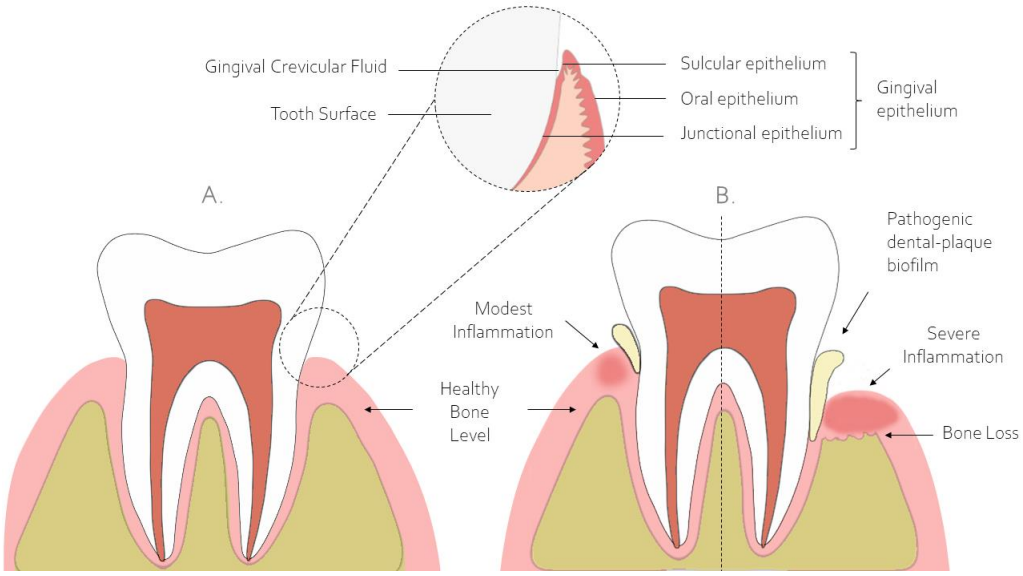


Figure 1 | ***The progression of periodontal disease.***
A) Periodontal health - the supporting tissues of the tooth roots (alveolar bone and connective tissue) are present, covered by the oral epithelium, and connected by the junctional epithelium to the surface of the tooth. Between the tooth and the epithelium, there is a gap, designated as the gingival sulcus, which is lined by the sulcular epithelium and filled with gingival crevicular fluid. B) Gingivitis (Left to the dotted line) - the accumulation of dental plaque triggers a reversible state of moderate periodontal inflammation, in the absence of bone loss. Periodontitis (Right to the dotted line) - the progressive accumulation of pathogenic dental plaque promotes the detachment of the junctional epithelium and consequently the loss of the connective tissue and alveolar bone (Original Image).

Periodontitis can cause swelling and bleeding of the soft tissues (gingiva and periodontal ligament), as well as tooth mobility in the absence of pain. Therefore, despite the destruction of the periodontium, it may advance as a 'silent disease' (Fischer et al., 2020). On that account, the early diagnosis and treatment of periodontitis, as well as the education of patients towards the self-perception of the disease, are crucial to prevent the negative impacts it has on OHRQoL, and to obtain control of the disease (Buset et al., 2016; Haag et al., 2017; Machado, Botelho, et al., 2020).

In addition to leading to tooth loss, periodontitis can also negatively impact the overall health by enhancing the patient's risk for a number of systemic diseases, such as cardiovascular diseases (Humphrey et al., 2008; Muñoz Aguilera et al., 2020), chronic kidney disease (Chambrone et al., 2013), diabetes mellitus (DM) (Chapple & Genco, 2013; Graziani et al., 2018), rheumatoid arthritis (Borgnakke, 2015), adverse pregnancy outcomes (Ide & Papapanou, 2013), aspiration pneumonia (Buset et al., 2016) and cancer (Whitmore & Lamont, 2014). Recently, periodontitis has been found to be correlated with polycystic ovary syndrome (Machado, Escalda, et al., 2020) and a higher risk of Covid-19 complications (hospital admissions, assisted ventilation or death) (Marouf et al., 2021; Shamsoddin, 2021).

1.2. Etiopathogenic Mechanisms

The host's innate immune system is constantly challenged by the microbial biofilm present in the gingival sulcus (Darveau, 2010). Since the epithelial cell surface of periodontal tissue lacks a significant mucous layer to prevent microbial contact, the host innate immune system requires an active maintenance of tissue homeostasis, which is essential for periodontal health (Darveau, 2010).

Large fluid-filled intracellular spaces emerge from the junctional epithelium, due to its high degree of porosity, as its cells are joined by a few desmosomes and the occasional gap junction. Therefore, an organized immune defense mechanism is mandatory to deal with the ongoing microbial stimulus (Darveau, 2010). In detail, neutrophils move from the highly vascularized gingival tissue to the gingival crevice, through the coordinated expression of e-selectin, intercellular adhesion molecules (ICAMs), and interleukin-8 (IL-8) to form a barrier between the host and the plaque biofilm (Darveau, 2010; Meyle & Chapple, 2015) (Figure 2).

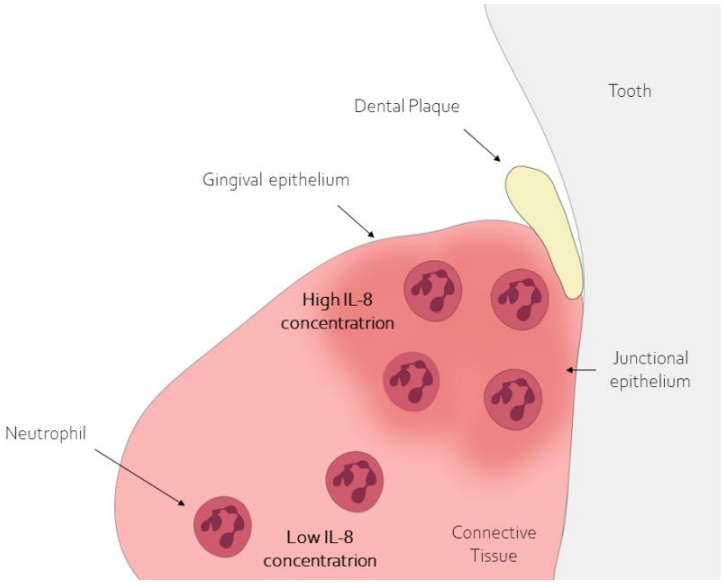


Figure 2 | ***The coordinated immune defense mechanism.***

In healthy periodontal tissues, the innate host defense status promotes the coordinated expression of defense mediators, like IL-8, which facilitates the transit of neutrophils across the tissue (Original Image).

Neutrophils are the most frequent leukocytes attracted to subgingival crevices or periodontal pockets, due to their importance for maintaining the homeostasis of periodontal tissue. However, if dysregulated and in excess can also be responsible for the destruction of the periodontium, since their local number is related to the severity of chronic periodontitis (Hajishengallis, 2015).

A triad of anaerobic periopathogens, denominated the" red complex" (*Porphyromonas gingivalis, Tannarella forsythia* and *Treponema denticola*), has shown a strong association with disease sites, as they may inhibit innate host defense functions. However, periopathogenic microorganisms are also detected in periodontally healthy individuals. In fact, recent studies support that the disease is caused by the polymicrobial dysbiosis and synergy of the periodontal tissues associated biofilm, rather than by single pathogens (Darveau, 2010; Hajishengallis, 2015).

To disrupt the oral microbiota, periopathogenic bacteria require the involvement of the commensal microbiota and the susceptibility of the host immune system, shifting the microorganisms, from Gram-Positive to Gram-Negative, and triggering the release of harmful host inflammatory cytokines (Darveau, 2010; Hajishengallis, 2015).

In healthy periodontal tissues the increase of the pro-inflammatory cytokines concentration can directly affect bone loss by raising the ratio of the receptor- activator of nuclear factor-kB ligand (RANKL)/ osteoprotegerin (OPG), allowing the RANKL to bind to RANK on osteoclast precursors. This causes the osteoclast precursors to develop into active macrophage-like cells that secret enzymes which break down bone (Darveau, 2010).

Briefly, the presence of bacterial products in the gingival sulcus causes the host's release of inflammatory mediators, increasing neutrophil migration to the gingival crevice, and so the junctional epithelium proliferation (referred to as "early gingivitis"). If the dental plaque buildup in the sulcus persists, the composition of the inflammatory infiltrate changes, progressing to an 'established gingivitis' and to 'periodontitis', with the thinning and ulceration of the junctional epithelium, causing more subgingival bacterial dissemination (Donos, 2018; Nibali, 2018) (Figure 3).

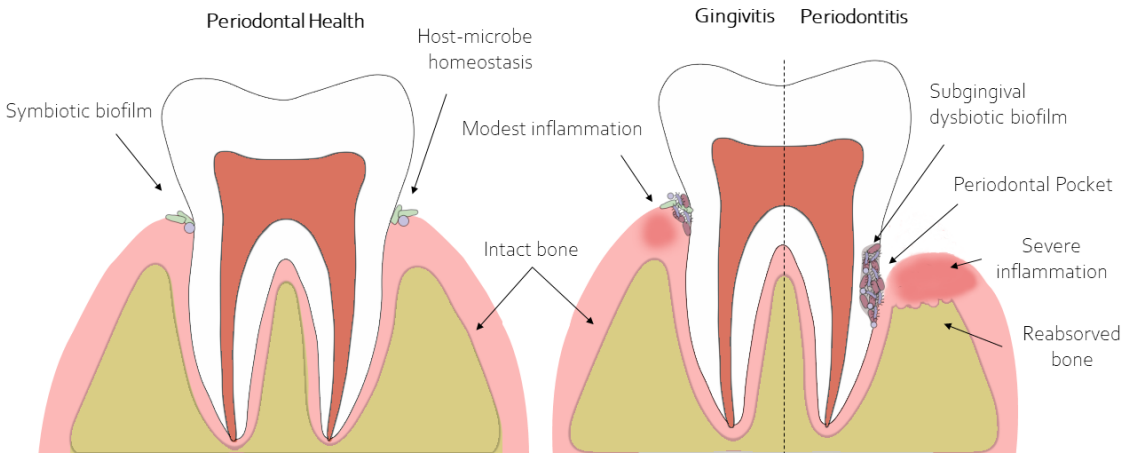


Figure 3 | ***Microbial Shift in Periodontitis.***

In a healthy periodontium (left), the subgingival symbiotic biofilm causes the host's innate immune system to mount an ongoing, defense response, which creates a state of homeostasis between the host and the microbiota. Howbeit, if supragingival dental plaque is consistently accumulated, a mild gingival inflammation, designated as gingivitis, typically develops (middle). Unless the dental plaque buildup is interrupted, over time in susceptible hosts, the commensal bacteria may cause a more severe inflammatory response, and consequently a microbial shift. This dysbiosis of the microbiota will manipulate the host's immune system, triggering the formation of periodontal pockets and alveolar bone loss – periodontitis (right) (Original Image).

Although the main etiological factor for periodontitis is dental plaque, many risk factors and indicators may enhance its progression and clinical presentation (Meyle & Chapple, 2015).

1.3. Causal and Risk Factors

An essential but frequently insufficient prerequisite for the establishment of periodontal disease is the persistent accumulation of dental plaque, particularly in the subgingival region (Genco & Borgnakke, 2013; Kinane et al., 2017). The dysbiosis alone may not precipitate periodontitis, however in conjunction with other risk factors and indicators, can alter an individual's immune system susceptibility and resistance (Hajishengallis, 2015).

The risk factors and indicators of periodontitis are often manageable (Bouchard et al., 2017). Those can be self-controlled or by health professionals, and comprise habits, for example smoking (Burt, 2005) and excessive alcohol consumption (Wang et al., 2016); and health issues, namely uncontrolled diabetes (Preshaw et al., 2012), obesity (Keller et al., 2015), osteopenia, stress, and insufficient intake of calcium and vitamin D (Bouchard et al., 2017; Humagain & Adhikari, 2018). Modifying these risk factors and

indicators is a conceptual topic to address in relation to periodontal disease management (Genco & Borgnakke, 2013).

On the contrary, non-modifiable risk factors and indicators namely age, gender, genetics, and ethnicity, cannot be changed, yet, they provide the knowledge to target specific interventions for patients with higher susceptibility (Bouchard et al., 2017).

2. PREVALENCE

Periodontitis represents a major issue on global public health (Dumitrescu, 2016). Past efforts to summarize the prevalence of periodontitis have shown that mild to moderate periodontitis is present in the majority of population, and severe periodontitis (SP) affects 11% of any population (Dye, 2012; Kassebaum et al., 2014; Petersen & Ogawa, 2012).

Patients with periodontal diseases, notably periodontitis, are more likely to have masticatory dysfunction, due to tooth mobility and tooth loss, all of which have a detrimental effect on their diet and confidence (Reynolds & Duane, 2018). Despite being generally preventable, easily diagnosed, and possibly efficiently managed, periodontal diseases are frequently disregarded by both individuals and health policy makers because they can advance, as a 'Silent disease', in the absence of pain, as previously mentioned (Chen et al., 2021; Tonetti et al., 2017).

The current trends of periodontitis are crucial to establish an effective public health policy (Chen et al., 2021). They supply the data needed to establish the priority targets for research, health policy, funding, and development to governments and domestic and non-governmental organizations (Kassebaum et al., 2014; Murray et al., 2012).

However, defining periodontitis in a replicable way demonstrates to be a difficult task, due to the many classifications developed, most of which have their own case definitions (Beltrán-Aguilar et al., 2012). A comparison of the data is hampered by the heterogeneity of case definitions, which can result in either an overestimation or an underestimating of disease prevalence (F. O. Costa et al., 2009).

2.1. Case Definitions

The full-mouth recording protocol (FRP) is considered to be the gold standard approach in periodontal clinical practice and research, in which all six sites of the tooth are probed, except for the third molars (Machado et al., 2018). However, in epidemiological studies its time consuming and labor intensive, which could result in dropout rates and measurement inaccuracies (Kingman et al., 2008; Machado et al., 2018). Consequently, multiple partial recording protocols (PRP) have been presented (Tran et al., 2013, 2014).

A recent study has shown that the 2018 European Federation of Periodontology/ American Academy of Periodontology (EFP/AAP) classification outperforms the 2012 Centers for Disease Control/ American Academy of Periodontology (CDC/AAP) classification regarding the periodontitis diagnosis and staging on full-mouth Partial Recording Protocols (PRPs) (Botelho et al., 2020; Eke, Page, et al., 2012; Tonetti et al., 2018). Given the challenges of using full-mouth protocols in epidemiological studies, the EFP/AAP 2018 classification on full-mouth partial recording protocols may enhance the population-based research on periodontal diseases (Botelho et al., 2020).

Implementing a consensus in the diagnostic criteria will improve the surveillance of periodontitis, as it allows for international comparability and for future national public strategies (Botelho et al., 2019).

3. AIMS

The present systematic review aims to thoroughly estimate the prevalence of periodontitis reported in studies between 2011 and 2020 sourced from epidemiological data. Our secondary objectives are to evaluate the prevalence geographically, to compare estimates from confident and non-confident case definitions, and to explore other confounding variables.

Hence, the addressed PECO question is as follows: "What is the pooled prevalence estimate of periodontitis in epidemiological studies carried out between 2011 and 2020?". accompanied by the following pillars:

- P (Population): Among subjects assessed in an epidemiological survey;
- E (Exposure): Periodontitis;
- C (Comparison): Periodontal status assessed;
- O (Outcome): Prevalence

II. MATERIAL AND METHODS

1. PROTOCOL AND REGISTRATION

The present systematic review protocol was previously developed by all of the authors and then submitted in the National Institute for Health Research PROSPERO, International Prospective Register of Systematic Reviews (http://www.crd.york.ac.uk/PROSPERO, ID Number: CRD42021231357). The review design followed the Cochrane Handbook of Systematic Reviews of Interventions (Higgins et al., 2019) and was reported following to the updated Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (M. J. Page et al., 2021). The PRISMA checklist is provided as a Supplemental information file (*Supplementary file 1 and 2*).

2. TYPE OF STUDIES, INTERVENTION, AND INCLUSION CRITERIA

The eligibility criteria were defined as: observational epidemiological studies (cross-sectional and cohort studies) reporting the prevalence of periodontitis in adults (18 years old or older), between 2011 and 2020 were eligible for inclusion. Cross-sectional and cohort studies (data was gathered from baseline reports) represent epidemiological studies in nature and provide prevalence traits important for the objectives of the present systematic review. Case-control studies were not considered due to the associated convenience in sampling cases and controls (Belbasis & Bellou, 2018). In line with this, intervention studies (both randomized and non-randomized) were only considered if they had a baseline inclusion of participants with an epidemiological approach.

In contrast, studies reporting the prevalence of periodontitis of a specific population (e.g., pregnant women, subjects with a particular underlying disease, etc.), studies based on self-reported case definitions of periodontitis, and preclinical studies were excluded.

In case of additional data clarifications, the corresponding author of the included study was contacted via e-mail, and again one week later.

3. PRIMARY AND SECONDARY OUTCOMES

The primary outcome of the present systematic review was the prevalence of periodontitis reported in epidemiological studies, either national or regional. We further explored the distribution of periodontitis per continent, according to the case definition, according to established age intervals, and according to the severity of periodontitis.

4. INFORMATION SOURCES SEARCH

The search strategy sought to identify all studies reporting the prevalence of periodontitis conducted between January 2011 and December 2020. We defined this year interval, given the recent estimates by Kassebaum et al. (Kassebaum et al., 2017) for the period comprised between 1990 and 2010.

Detailed search strategies were conducted without language restrictions, on the following electronic databases: PubMed, Web of Science and LILACS (Latin-American scientific literature in health sciences). The search algorithm, developed using keywords and the Medical Subject Headings (MeSHs), was: "(periodont* OR "chronic periodontitis" OR (periodontal diseases [MeSH]) OR "attachment loss" OR pocket*) AND (prevalence [MeSH] OR epidemiology [MeSH])". For the remaining databases the search was adapted accordingly.

5. STUDY SELECTION

Two researchers (D.T. and L.C.) independently selected the relevant articles by screening the titles and abstracts, excluding the non-relevant studies. The papers that were classified as potentially eligible by either reviewer was appraised by a full-text reading, and the reasons for exclusion were fully detailed. Any disagreement was resolved through discussion with a third reviewer (J.B.) and a decision arrived at by consensus.

6. DATA EXTRACTION PROCESS AND DATA ITEMS

The studies that fulfilled the inclusion criteria were organized into evidence tables describing the characteristics and results of each study, including: study identification (i.e., first author's name and publication year), time period of the study, continent, country of origin of the research, country coordinates, funding information, inclusion and exclusion criteria, periodontal case definition, characteristics and number of participants; outcome measures. We later added the methodological risk of bias of the study (detailed in 7. Risk of bias assessment). All disagreements were discussed and settle with a third reviewer (JB). Due to the known impact of case definitions in prevalence estimates (Holtfreter et al., 2015) , we have categorized case definitions following the strategy used by Muñoz Aguilera et al. (Muñoz Aguilera et al., 2020) as confident and non-confident,, as explained below.

6.1. Confident Case Definition of Periodontitis

The following case definitions were considered as confident:

- Interdental clinical attachment loss (CAL) at ≥2 non-adjacent teeth, or buccal or oral CAL ≥3 mm with periodontal probing depth (PPD) >3 mm is detectable at ≥2 teeth – American Academy of Periodontology (AAP) / European Federation of Periodontology (EFP) (Tonetti et al., 2018);

- Two or more interproximal sites with CAL ≥3 mm and two or more interproximal sites with PPD ≥4 mm (not on the same tooth) or one site with PPD ≥5 mm – Centre for Diseases Control (CDC)/AAP 2012 (Eke, Page, et al., 2012);

- At least two sites on different teeth with clinical attachment level (CAL) 6 mm and at least one site with PPD 4 mm – CDC/AAP 2007 (R. C. Page & Eke, 2007);

- Generalized chronic periodontitis (at least 30% sites with CAL ≥ 4 mm) – CDC 1999 (Armitage, 1999).

6.2. Non-confident Case Definition of Periodontitis

The following reported criteria were considered as a non-confident case definition: the World Health Organization (WHO) Community Periodontal Index (CPI), score 3/4 in at least one quadrant; at least one site with PPD >4mm; Clinical Attachment Loss ≥1mm.

7. RISK OF BIAS ASSESSMENT

The methodological quality of the included studies was carried out by two reviewers independently (DT and LC), applying the "Assessing risk of bias in population-based prevalence studies" tool (Hoy et al., 2012). All disagreements were discussed and settle with a third reviewer (JB).

The tool consists of 10 items addressing: external validity (items 1 to 4 - accounting the selection and non-response bias domains); and internal validity (items 5 to 10 - accounting the measurement bias and bias related to the analysis domains). Each item was rated as either 'yes' (low) or 'no' (high) risk of bias. Items regarding insufficient information to properly meet its requirements were classified as 'no' (that is, high risk of bias) (Hoy et al., 2012). Considering the instruction of Hoy et al., the overall risk of bias of each study was decided in agreement with all authors. Therefore, each article overall risk of bias was evaluated as of: 'High' – If only 0 to 3 items were responded with yes, having an important impact on our confidence in the estimate, and will likely change the estimate; 'Moderate' – If 4 to 8 items were responded with yes; and, 'Low' – If 9 or more items were responded with yes, indicating that further research is very unlikely to change our confidence in the estimate.

8. STATISTICAL ANALYSIS

Extracted data was organized into evidence tables. Due to the existence of multiple category prevalence for periodontitis in literature, and the possible affected variance possibly in imbalance weight of the studies in the meta-analysis, we implemented a double arcsine transformation meta-analysis (Barendregt et al., 2013). Considering the geographic variation and discrepancy in populations, we could not assume the existence of a true effect size, thus we employed a random effects model (Schwarzer et al., 2015), as previously described (Schwarzer, 2007). All random-effects meta-analysis and forest plots were performed in R version 3.4.1 using 'meta' package (Schwarzer, 2007). The results are presented as percentage prevalence ($p \times 100\%$) and 95% confidence intervals (CI). Heterogeneity was explored through the I2 index and Cochrane's Q statistic ($p<0.1$), and $\chi 2$ test for the overall homogeneity (Higgins et al., 2019). Substantial heterogeneity was defined as $I2 > 50\%$. All tests were two-tailed, with alpha set at 0.05.

We conducted a series of a priori sensitivity analyses (that is, subgroup analyses) to examine the effect of the case definition confidence (confident versus non-confident) and risk of bias (low versus moderate-high) to the overall estimates. Meta-regression was used to explore adjusting effects particular confounding variables on the prevalence estimates, particularly female/male ratio, latitude, longitude and study sample size.

III. RESULTS

1. STUDY SELECTION

The electronic searches retrieved a total of 5,755 records (1,942 from PubMed, 3,023 from Web of Science, and 790 from LILACS). After duplicates removal, 4,968 articles were excluded based on the title and abstract assessment and 28 articles were unable to access. Out of the articles remaining, 352 articles were excluded in the full-text appraisal, due to not meeting the inclusion criteria, with the respective reason detailed in PRISMA (M. J. Page et al., 2021) (Figure 4). Finally, a total of 83 articles, were included in the qualitative and quantitative analyses of the present systematic review (Figure 4). Data from two studies were reported in multiple articles, so these papers were combined under a single as showed:(Bhat et al., 2015, 2018; Eke et al., 2015, 2018). Therefore, a final sample of 81 articles was included. Inter-examiner reliability at full-text screening was rated as excellent (kappa score = 0.86, 95% CI: 0.83–0.89).

One study did not report data for the overall prevalence of periodontitis, but reported data for the subgroup analysis information of moderate-to-severe periodontitis (Ha et al., 2020). To complete information to the year range of interest, we used the official report where this information was detailed (ARCPOH, 2019).

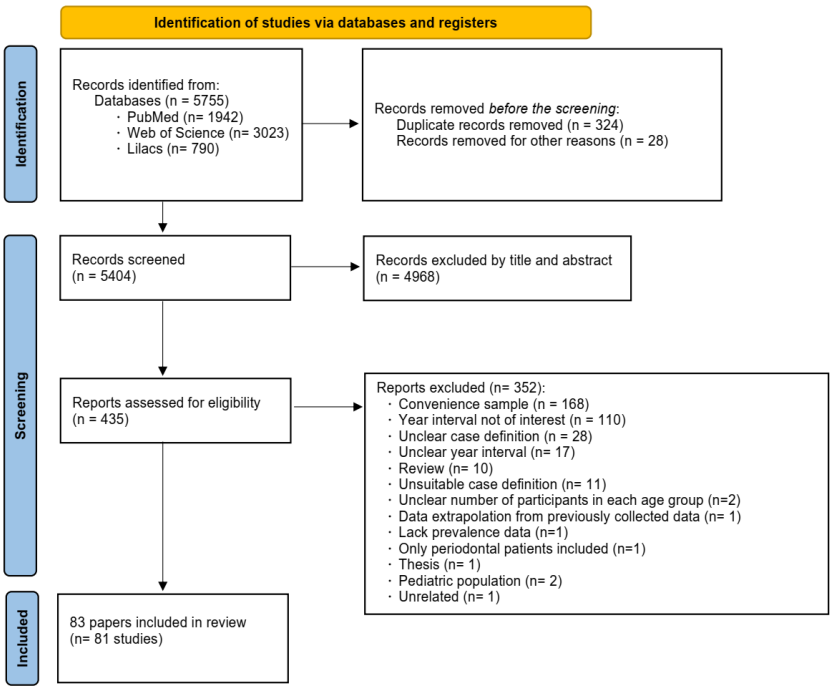


Figure 4 | ***Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flowchart of studies inclusion***

2. STUDY CHARACTERISTICS

Table 1 summarises the study characteristics by chronological order of the included studies. Studies from twenty-five different countries across Asia, America, Europe Australia and Africa were included. Most studies (n=49, 61.3%) (Balaji et al., 2018; Castrejón-Pérez et al., 2017; Clauss et al., 2021; P. D. Costa et al., 2021; Dhaifullah et al., 2019; Díaz-Reissner et al., 2020; Giacaman et al., 2016; D. H. Han & Kim, 2021; K. Han & Park, 2017; S. J. Han et al., 2019; Holtzman et al., 2017; J. W. Hong et al., 2016; M. Hong et al., 2016; T. Iwasaki et al., 2018; Jaafar et al., 2014; Jeong et al., 2020; Jiao et al., 2021; Juarez et al., 2015; Jung et al., 2019; Khan et al., 2016; Kim et al., 2019; Konopka et al., 2015; Kwon et al., 2018; Lasta et al., 2019; E. Lee & Lee, 2019; K. Lee & Kim, 2019; S.-W. Lee et al., 2017; Moya et al., 2014; Nakamura et al., 2020; Pinto-Filho et al., 2018; Ra et al., 2020; Sakurai et al., 2021; Schmidt et al., 2020; Sekiguchi et al., 2020; Shimizu et al., 2019; Shyagali et al., 2017; Silva-Junior et al., 2017, 2019; Sim et al., 2017; Singh et al., 2020; E. Song et al., 2021; Su et al., 2021; Sun et al., 2020; Suominen et al., 2018; Vano et al., 2015; Wahlin et al., 2018; Zaitsu et al., 2017; Zhao et al., 2019) reported periodontal outcomes using a non-confident case definition, either the community periodontal index (CPI) score 3/4 in at least one quadrant, at least one site with PPD >4mm, or clinical attachment loss ≥1mm. Within the confident periodontal definitions, the CDC/AAP 2012 was the most employed, being reported in 18 studies (22.5%) (Bhat et al., 2015, 2018; Cepeda et al., 2017; Germen et al., 2021; Ghassib et al., 2021; Goel et al., 2021; Gomes-Filho et al., 2021; He et al., 2018; Helmi et al., 2019; Holde et al., 2017; M. Iwasaki et al., 2021; Kotsakis et al., 2015; Machado et al., 2021; Oliveira et al., 2021; Papapanou et al., 2020; Shariff et al., 2017, 2018; Skoskiewicz-Malinowska et al., 2018; Y. H. Song et al., 2021; Vallespir et al., 2014), and the remaining reported periodontitis based on confident case definitions.

Table 1 | ***Studies Characteristics***

Authors (year) (country)	Inclusion criteria	Exclusion Criteria	Periodontal criteria (confidence)	Periodontal Examination Protocol	Periodontitis / Healthy (n)	Age interval (years)	Male / Female	Funding source
(Moya et al., 2014) (Chile)	≥60 years old, beneficiary of the public health system, and assisted at the health center at east Santiago of Chile	NR	CPI (Non-Confident)	Partial-mouth (CPI)	168/212	≥60	NR	NR
(Figueiredo et al., 2013) (Brazil)	Kiriri Indians aged 19 years and older who were living in an isolated Indian area in the state of Bahia, in Northeast Brazil	Cardiovascular diseases and other conditions that require antibiotics before periodontal probing	CDC/AAP 2007 (Confident)	Full-mouth (6 sites)	85/130	≥19	96/119	Research Grant
(Thanakun et al., 2014) (Thailand)	NR	Patients with systemic diseases, as well as those who had received medications	Armitage 1999 (Confident)	Full-mouth (6 sites)	90/35	35-76	53/72	Research Grant
(Jaafar et al., 2014) (Malaysia)	≥19 years old	NR	CPI (Non-Confident)	Partial-mouth (CPI)	228/ 309	≥19	218/319	Research Grant
(Vallespir et al., 2014) (Chile)	35-44 years old, belonging to the family health center Lorenzo Arenas from the municipality of Concepción, Chile	NR	CDC/AAP 2012 (Confident)	Full-mouth (6 sites)	32/26	35-44	NR	NR
(Kotsakis et al., 2015) (USA)	NR	Missing clinical periodontal data, aspirin users who did not satisfy our definition of low-dose aspirin use, or who did not complete the preventive aspirin use questionnaire	CDC/AAP 2012 (Confident)	Full-mouth (l6 sites)	1.406/929	40-80	NR	Research Grant

(Juarez et al., 2015) (Chile)	18-70 years old, ≥2 teeth in the mouth	Pregnant, underwent periodontal treatment during the last 6 months, undergoing current periodontal treatment, on antibiotic treatment for a week or more in the last 6 months, or on treatment with immunosuppressive agents, all conditions that alter the periodontal status; antibiotic consumption for 7 days in the past 6 months, the current consumption of nifedipine, >70 years old and presented abdominal hernia	PPD ≥ 4mm (Non-Confident)	Full-mouth (6 sites)	67/69	18-70	51/85	NR
(Vano et al., 2015) (Italy)	≥18 years old	NR	CPI (Non-Confident)	Partial-mouth (Sextants)	38/ 312	≥18	161/189	NR
(Konopka et al., 2015) (Poland)	65-74 years old	Only 1 tooth in the sextant or edentulous	CPI (Non-Confident)	Partial-mouth (Sextants)	335/ 472	65-74	NR	NR
(J. W. Hong et al., 2016) (Republic of Korea)	≥ 19 years old	NR	CPI (Non-Confident)	Partial-mouth (Sextants)	2,728/ 7,249	≥19	4,306/5,671	NR
(Khan et al., 2016) (Pakistan)	≥18 years old	Participants who had received periodontal treatment in the last 4 months, participants on antibiotics within the past 4 months, pregnant women and lactating mothers, mentally handicapped, or on prophylactic antibiotics, or systemic/topical steroidal anti-inflammatory drugs for the last 4 months.	CPI (Non-Confident)	Partial-mouth (Sextants)	310/133	≥18	287/156	Self-funded
(M. Hong et al., 2016) (Republic of Korea)	≥30 years old	NR	CPI (Non-Confident)	Partial-mouth (FDI Index teeth)	1,272/ 3,205	≥30	2,231/2,246	NR

(Giacaman et al., 2016) (Chile)	The entire population of the Maule Region, divided according to the ages of epidemiological surveillance indicated by the WHO, that is, 6, 12, 15, 35 to 44 and 65 to 74 years	Systemic conditions that contraindicate periodontal evaluation, people who suffered heart disease, bleeding disorders or were under anticoagulant drug therapy, and all participants who were within the study ages but suffered from some cognitive deficit or disability mental	CPI (Non-Confident)	Partial-mouth (CPI)	162/ 531	35-44; 65-74	124/ 569	Research Grant
(Castrejón-Pérez et al., 2017) (México)	NR	NR	Modifed periodontal screening and recording index, measuring six sites per tooth and recording the highest score on each tooth; severe periodontitis was indicated by the presence of at least three teeth with ≥5.5-mm pocket depth and furcation involvement or ≥3.5-mm gingival recession (Non-Confident)	Full-mouth (Most severe site per tooth)	49/139	≥70	NR	Research Grant

(Holtzman et al., 2017) (USA)	≥ 18 years old; had no cognitive, vision, or hearing difficulties that interfered with their ability to complete the survey; were not working or training in the health care field; had fewer than five visits to the dental school; or if they were former patients of the school, had no dental visit at the school for more than 5 years.	NR	PPD ≥ 4mm (Non-Confident)	Full- mouth (Most severe site per tooth)	295/ 30	≥18	178/ 149	Research Grant
(Ramírez et al., 2017) (Colombia)	≥ 35 years old, full clinical history and periodontal chart, presence of at least 10 teeth in the mouth excluding third molars.	NR	Armitage 1999 (Confident)	Full-mouth (6 sites)	314/ 153	≥35	112/ 355	NR
(Shariff et al., 2017) (USA)	30-59 years old	Edentulous	CDC/AAP 2012 (Confident)	Full-mouth (6 sites)	1,660/ 278	30-59	NR	NR
(Sim et al., 2017) (Republic of Korea)	≥19 years old	NR	CPI (Non-confident)	Partial-mouth (FDI Index teeth)	4,225/ 10, 468	≥19	7, 296/ NR	NR
(Zaitsu et al., 2017) (Japan)	Adults aged 19 – 70 years old employed at 11 companies (Company A-K) in the Kanto region of Japan	NR	CPI (Non-confident)	Partial-mouth (Sextants)	109/ 969	19-70	798/ 270	Research Grant
(K. Han & Park, 2017) (Republic of Korea)	NR	Participants younger than 19, participants 40 or older, individuals with pregnancy or menopause	CPI (Non-confident)	Partial-mouth (CPI)	329/ 3,496	19-39	2,097/ 1,728	Research Grant
(Cepeda et al., 2017) (USA)	Subjects ≥ 30 years old who underwent a periodontal examination and responded to the question about the frequency of flossing	NR	CDC/AAP 2012 (Confident)	Full-mouth	3,374/ 3,565	≥30	NR	Company Grant

(S.-W. Lee et al., 2017) (Republic of Korea)	≥19 years old	NR	CPI (Non-confident)	Partial-mouth (Sextants)	1,554/ 4,422	≥19	NR	Research Grant
(Silva-Junior et al., 2017) (Brazil)	Adults aged between 20 and 64 years.	NR	CPI (Non-confident)	Partial-mouth (Sextants)	107/ 141	20-64	NR	Research Grant
(Shyagali et al., 2017) (India)	Subjects who were indulged in the usage of tobacco products more than four times a week and for not less than a year	Subjects who consumed any of the tobacco products less than four times a week, who had a systemic disease and who were on medication for such diseases	CPI (Non-confident)	Partial-mouth (CPI)	143/ 337	18-50	NR	NR
(Holde et al., 2017) (Norway)	Adults aged 20-79 years old, living in Troms County, Norway	Edentulous or only one tooth	CDC/AAP 2012	Full-mouth (6 sites)	946/ 965	20-79	1,016/ 895	Research Grant
(Kwon et al., 2018) (Republic of Korea)	≥ 20 years old	Missing data for at least one of the following categories: blood samples, anthropometric variables, or oral examination	CPI (Non-confident)	Partial-mouth (FDI Index teeth)	3,568/ 8,681	≥20	4,941/ 7,308	Self-funded
(Suominen et al., 2018) (Finland)	≥ 30 years old	NR	PPD ≥ 4mm (Non-Confident)	Full mouth (4 sites – Distal, Mid Buccal, Mid Lingual, Mesial)	860/ 497	≥30	609/ 748	Research Grant
(He et al., 2018) (China)	Subjects within the 35 to 44, 55 to 64, and 65 to 74 years age groups, had the ability to understand and answer the questionnaire, and had lived in the selected communities or villages for more than 6 months in the past year.	Subjects from 45 to 54 years age group, undergoing orthodontic treatment, teeth were covered by lots of calculus	CDC/AAP 2012 (Confident)	Full-mouth	296/ 184	35-44; 55-64; 65-74	243/ 237	Research Grant
(T. Iwasaki et al., 2018) (Japan)	NR	Participants who had chronic hepatitis C infection and chronic hepatitis B infection	PPD ≥ 4mm (Non-Confident)	Full-mouth (6 sites)	941/ 285	40-59	NR	Self-funded

(Ortiz et al., 2018) (Puerto Rico)	NR	History of clinically diagnosed diabetes, less than four natural teeth, a history of conditions that increase the risk of systemic complications during a periodontal exam, and inability to complete study procedures, fasting, two-hour glucose, or HbA1c levels met the American Diabetes Association thresholds for diabetes at the baseline exam	CDC/AAP 2007	Full-mouth (6 sites)	438/ 297	41-70	204/ 531	Research Grant
(Bhat et al., 2015, 2018) (India)	Participants aged 35-54 years, dentate	Any participant reporting medical conditions (uncontrolled diabetes, heart disease, bleeding disorders) that contra-indicated periodontal probing	CDC/AAP 2012	Full-mouth (6 sites)	405/ 464	35-54	472/ 397	NR
(Balaji et al., 2018) (India)	≥ 18 years old	Participants who were pregnant, mentally ill, edentulous, not ambulatory, or critically ill	CAL ≥1 mm (Non-Confident)	NR	423/ 577	≥18	NR	Research Grant
(Eke et al., 2015, 2018) (USA)	Adults 30 years or older who had 1 or more natural teeth and no health conditions requiring antibiotic prophylaxis before periodontal probing	Medical conditions, Incomplete oral examinations and institutionalized participants	CDC/AAP 2012 (Confident)	Full-mouth (6 sites)	3320/3620	≥30	NR	NR

(Pinto-Filho et al., 2018) (Brazil)	Kiriri Indians aged ≥ 19 years living in an isolated area in Bahia state, northeast Brazil	Patients with missing information	Severe periodontitis ≥ 2 proximal sites CAL ≥ 6 mm, not on the same tooth, and ≥ 1 proximal site with a PPD ≥ 5 mm. (Non-Confident)	Full-mouth (6 sites)	65/ 160	≥19	101/ 124	Research Grant
(Shariff et al., 2018) (USA)	≥ 65 years old	NR	CDC/AAP 2012 (Confident)	Full-mouth (6 sites)	691/ 169	≥65	NR	Research Grant
(Skoskiewicz-Malinowska et al., 2018) (Poland)	≥ 65 years old, local resident, able to communicate, and a written consent to participate in the survey	Coexisting systemic diseases in which dental pocket probing leading to transient bacteremia might have posed a risk for the patient's overall health condition: cardiovascular diseases (patients with heart valves, after heart transplant, with congenital heart diseases, or with infective endocarditis), blood diseases (thrombocytopenia, hemophilia, von Willebrand disease), viral diseases (B and C type hepatitis, AIDS/HIV), as well as patients with Multi-Drug Resistant Organisms (MDRO) , as well as lack of a written consent, or mental disorders	CDC/AAP 2012 (Confident)	Full-mouth (6 sites)	448/ 52	≥65	NR	Research Grant

(Wahlin et al., 2018) (Sweden)	20-80 years old	Edentulous and if they had any type of implants or prosthesis	PPD ≥ 4mm (Non-Confident)	Full -mouth (4 sites – mesial, mid buccal, midl ingual, mesial)	248/ 373	20-80	NR	NR
(Montero et al., 2019) (USA)	Participants aged ≥30 years with the following registered data: age, gender,ethnicity, smoking habit, BMI, blood pressure, total cholesterol and HbA1c having >14 teeth and having received a periodontal examination.	NR	CDC/AAP 2007 (Confident)	Full-mouth (6 sites)	1,516/ 1,501	≥30	1,516/ 1,501	Research Grant
(Jung et al., 2019) (Republic of Korea)	≥19 years old	NR	CPI (Non-Confident)	Partial-mouth (Sextants)	4,335/ 9,929	≥19	6,046/ 8,218	NR
(Zhao et al., 2019) (China)	≥30 years old	NR	CPI (Non-Confident)	Partial-mouth (CPI)	403/ 3, 549	30-68	NR	NR
(K. Lee & Kim, 2019) (Republic of Korea)	≥30 years old	NR	CPI (Non-Confident)	Partial-mouth (Sextants)	2,771/ 7,027	≥30	3,717/ 6,081	Company Grant
(Silva-Junior et al., 2019) (Brazil)	Piracicaba residents aged 20–64 years old, mentally capable to answer the study questionnaire and agreeing to participate in the research	A physical or psychological state that prevented the achievement of clinical procedures or understanding of the questionnaire	PPD ≥ 4mm (Non-Confident)	Partial mouth	43/ 100	20-64	NR	Research Grant
(Kim et al., 2019) (Republic of Korea)	Adults aged 35-79 years old	NR	CPI (Non-Confident)	Partial-mouth (Sextants)	3,098/ 5,216	35-79	NR	Research Grant

(Lasta et al., 2019) (Brazil)	≥60 years old	NR	CPI (Non-Confident)	Partial-mouth (Sextants)	3/ 47	≥60	NR	NR
(E. Lee & Lee, 2019) (Republic of Korea)	40-79 years old	NR	CPI (Non-Confident)	Partial-mouth (Sextants)	9,357,475/ 16,049,744	40-79	NR	Research Grant
(S. J. Han et al., 2019) (Republic of Korea)	≥19 years old	NR	CPI (Non-Confident)	Partial-mouth (FDI Index teeth)	4,110/ 5,618	≥19	4,110/ 5,618	NR
(Botelho et al., 2019) (Portugal)	≥18 years old (adults and elderly), living in the municipalities of Almada and Seixal	NR	EFP/AAP 2018	Full-mouth (6 sites)	637/ 427	18-95	447/ 617	Self-funded
(Helmi et al., 2019) (Saudi Arabia)	≥18 years old	Patients that were not within the specified age range, with no BW radiographs, with radiographs in which the cement-enamel junction (CEJ) and alveolar bone crest were not visible, who did not have at least 2 approximating teeth or where the interproximal space was too narrow to observe the bone crest	CDC/AAP 2012	Full-mouth (2 sites – Mesial and Distal)	893/ 238	≥18	508/ 623	Research Grant
(Shimizu et al., 2019) (Japan)	60-99 years old	Participants without data on carotid intima-media thickness (CIMT) and those without any remaining teeth	"ADVANCED" PPD ≥ 6.0 mm (Non-Confident)	Full-mouth (2 sites – Mesial-buccal and mid-buccal	197/ 710	60-99	353/ NR	Research Grant
(Dhaifullah et al., 2019) (Saudi Arabia)	18-40 years old At least 20 natural teeth	Pregnancy, periodontal treatment within the past 4 months, a history of systemic diseases or medications known to affect periodontal health status (i.e. diabetes, topical or systemic corticosteroids use, and/or antibiotics intake).	CPI (Non-Confident)	Parital-mouth (Sextant)	25/ 283	18-40	154/ 154	Self-funded

(Jeong et al., 2020) (Republic of Korea)	NR	< 19 years old	CPI (Non-Confident)	Partial-mouth (CPI)	4,260/ 9,291	≥19	5,715/ 7,836	NR
(Sun et al., 2020) (China)	55–74 years old, who had lived longer than 6 months in the sampling areas	Those who withheld consent or had serious diseases.	PPD ≥ 4mm (Non-Confident)	Full-mouth	6,066/ 2,988	55–74	4,514/ 4,540	Research Grant
(Bongo et al., 2021) (Norway)	Adults in Finnmark County in Northern Norway	Missing questionnaire, missing clinical data or both, unknown target age, missing written consent, or not accounted for and thus given missing unknown status	EFP/AAP 2018 (Confident)	Full-mouth (6 sites)	1,032 / 1,046	18–75	894 / 1,184	Research Grant
(Ra et al., 2020) (Republic of Korea)	≥50 years old	< 50 years old; not working	CPI (Non-Confident)	Partial-mouth (CPI Index teeth)	1,582/ 1,738	≥50	1,779/ 1,543	Research Grant
(Jung et al., 2020) (Republic of Korea)	≥40 years old	NR	CPI (Non-Confident)	Partial-mouth (Sextants)	3,725/ 3,994	≥40	NR	Self-funded
(Alqaderi et al., 2020) (USA)	≥30 years old	Health conditions that required antibiotic prophylaxis before periodontal testing	≥2 interproximal sites with CAL ≥6 mm, and ≥1 interproximal site with PPD ≥5 mm (Non-Confident)	Full-mouth (6 sites)	317/ 3,307	≥30	1,755/ 1,869	Self-funded
(Romero-Castro et al., 2020) (México)	18-75 years old, who reside in the state of Guerrero, Mexico	Pregnant or lactating women, as well as patients with systemic diseases or aggressive periodontitis	Armitage 1999 (Confident)	NR	98/ 63	18-75	NR	NR

(Ha et al., 2020) (Australia)	NR	Required antibiotic prophylaxis before dental check-up, Congenital Heart Murmur, Heart valve Problems, Congenital Heart Disease, Bacterial Endocarditis, Rheumatic Fever, Kidney Disease, Haemophilia, Pacemaker or Automatic defibrillator, Hipbone or joint replacement, transplanted organs	CDC/AAP 2012 (Confident)	Full-mouth (3 sites- Mesio-buccal, Mid-buccal, disto-buccal)	1,719/2,073	≥34	1,854/2,011	Research Grant
(Schmidt et al., 2020) (Switzerland)	≥55 years old	Edentulous participants; endocarditis	PPD ≥ 4mm (Non-Confident)	Partial-mouth (FDI Index teeth)	614/ 840	≥55	NR	Research Grant
(Nakamura et al., 2020) (Japan)	≥20 years old	Immunocompromised patients (i.e: patients who received chemotherapy, those with severe immunodeficiency, and those with autoimmune disease, who received immunosuppressant therapies)	PPD ≥ 4mm (Non-Confident)	Full-mouth	115/ 75	≥20	NR	Research Grant
(Papapanou et al., 2020) (USA)	Dentate individuals	NR	CDC/AAP 2012 (Confident)	Full-mouth (6 sites)	587/ 152	≥65	NR	Research Grant
(Singh et al., 2020) (Nepal)	35-44; 65- 74 years old	Psychiatric illness	CPI (Non-Confident)	Partial-mouth (CPI)	21/ 96	35-44; 65-74	NR	Self-funded
(Sekiguchi et al., 2020) (Japan)	≥18 years old	The participants without all oral examinations, those whose measured probing pocket depth (PPD) and clinical attachment loss (CAL) were not measured those without General Oral Health Assessment Index (GOHAI) scores, and those who underwent health check-ups more than two times in the 3-year period.	PPD ≥ 4mm (Non-Confident)	Full-mouth (2 sites- Mesio-Buccal and mid-buccal)	594/ 589	≥18	NR	Research Grant

(Díaz-Reissner et al., 2020) (Paraguay)	18-59 years old, Paraguayans and foreign nationals with more than 14 years of residence in the country	NR	CPI (Non-Confident)	Partial-mouth (Ramfjört teeth)	19/ 310	18-59	NR	Self-funded
(Sakurai et al., 2021) (Japan)	Individuals insured by the national health insurance system (including self-employed workers, farmers, and the elderly) and aged 30 years and older.	NR	CPI (Non-Confident)	Partial-mouth (CPITN)	1,907/ 2,199	≥30	NR	Research Grant
(Jiao et al., 2021) (China)	35-45; 55-65; 65-75 years old	NR	EFP/AAP 2018 (Confident)	Full-mouth (Most severe site)	8,391/ 4,804	35-45; 55-75	NR	Research Grant
(Goel et al., 2021) (Nepal)	20-65 years old, tobacco users who were currently consuming tobacco in the form of smoking or smokeless tobacco, non-tobacco users who had never used tobacco in any form (smoke or smokeless tobacco).	Former smokers, patients who actively consume alcohol, patients suffering from known systemic illness, pregnant and lactating females.	CDC/AAP 2012 (Confident)	NR	315/ 125	20-65	186/ 254	Self-funded
(Germen et al., 2021) (Turkey)	35-74 years old	Individuals who required antibiotics after routine periodontal procedures	CDC/AAP 2012 (Confident)	Full-mouth (6 sites)	302/ 186	35-74	NR	Self-funded
(D. H. Han & Kim, 2021) (Republic of Korea)	40-80 years old	Aged < 40 years, edentate, and those missing values in the health assessment or questionnaires.	CPI (Non-Confident)	Partial-mouth (FDI Index teeth)	3,339/ 4,988	40-80	3,572/ 4,755	Self-funded
(P. D. Costa et al., 2021) (Brazil)	≥18 years old At least 8 natural teeth	People with mental health disorders, under orthodontic treatment, and pregnant women	CPI (Non-Confident)	Partial-mouth (Sextants)	304/146	≥18	NR	Research Grant

(Y. H. Song et al., 2021) (Republic of Korea)	Six or more natural teeth	NR	CDC/AAP 2012 (Confident)	Full-mouth (2 sites – mesial and distal))	270/143	47-86	NR	Research Grant
(Gomes-Filho et al., 2021) (Brazil)	>18 years old, registered in basic health units	Diagnosed with neoplasia, HIV, pregnancy, required antibiotic prophylaxis prior to periodontal examination, used anti-inflammatories in the previous 6 months before the examination, received prior periodontal treatment or used antibiotics 6 months before the examination	CDC/AAP 2012 (Confident)	Full-mouth (6 sites)	851/160	≥18	332/ NR	Research Grant
(Machado et al., 2021) (USA)	≥18 years old, who received periodontal examination and answered the dietary interview for the total nutrient intakes	NR	CDC/AAP 2012 (Confident)	Full-mouth (6 sites)	3,976/2,973	≥18	NR	Research Grant
(Oliveira et al., 2021) (Brazil)	NR	Requirement of antibiotic prophylatic, psychiatric or mental problems, less than two teeth, less than 18 years old, presenting clinical attachment loss in two adjacent teeth	CDC/AAP 2012 (Confident)	Full-mouth (6 sites)	519/66	≥18	NR	Research Grant
(Clauss et al., 2021) (Burkina Faso)	35-44 years old, member of a randomly chosen household within the HDSS Household Survey in in Nouna	NR	CPI (Non-Confident)	Full-mouth (6 sites)	341/86	35-44	NR	Research Grant

(Su et al., 2021) (Japan)	Smokers and patients with a medical history of hypertension, diabetes, hyperlipidemia, stroke, heart disease, or bone and joint disease.	Subjects with oral cancer or potentially malignant oral disorders (i.e., leukoplakia or lichen planus), cancer patients receiving surgical treatment, chemotherapy or radiotherapy, those with auto-immune diseases receiving steroid therapy and those with severe immunodeficiency.	PPD ≥ 4mm (Non-Confident)	Full-mouth (6 sites)	72/52	35-90	NR	Research Grant
(Ghassib et al., 2021) (USA)	Participants underwent medical history screening, were 30-79 years old, had natural teeth, were not in need of prophylactic antibiotics, and provided informed consent for the oral examination.	<6 natural teeth (to ensure adequate representation of dentition)	CDC/AAP 2012 (Confident)	Full-mouth (6 sites)	862/360	30-79	NR	Self-funded
(M. Iwasaki et al., 2021) (Japan)	At least 18 years of age and able to read and understand Japanese.	Having fewer than 2 teeth and previous diagnosis of a severe or terminal disease, such as advanced heart failure, end-stage kidney disease, or advanced-stage cancer.	CDC/AAP 2012 (Confident)	Full-mouth (6 sites)	118/81	19-77	NR	Research Grant
(Stødle et al., 2021) (Norway)	≥ 19 years old and residents of the county	No radiographs, edentulous,	EFP/AAP 2018 (Confident)	Full-mouth (6 sites)	3.573/1.290	≥19	NR	Research Grant
(E. Song et al., 2021) (Republic of Korea)	Participants without previous thyroid disease or ongoing thyroid-related medication	NR	CPI (Non-Confident)	Partial-mouth (FDI Index teeth)	1,423/ 4,045	≥18	NR	Research Grant
(Bilgin Çetin et al., 2021) (Turkey)	NR	Patients younger than 18 years, edentulous patients	EFP/AAP 2018 (Confident)	Full-mouth (6 sites)	221/ 320	≥18	252/ 289	Research Grant

AAP – American Academy of Periodontology; CAL- Clinical Attachment Level; CDC – Centers for Disease Control; CPI – Community Periodontal Index; EFP – European Federation of Periodontology; NR – Not Reported; PPD – Periodontal Probing Depth

3. RISK OF BIAS

Sixty one (Alqaderi et al., 2020; Balaji et al., 2018; Bhat et al., 2015, 2018; Bilgin Çetin et al., 2021; Bongo et al., 2021; Castrejón-Pérez et al., 2017; P. D. Costa et al., 2021; Dhaifullah et al., 2019; Díaz-Reissner et al., 2020; Germen et al., 2021; Giacaman et al., 2016; Goel et al., 2021; Gomes-Filho et al., 2021; D. H. Han & Kim, 2021; K. Han & Park, 2017; S. J. Han et al., 2019; Helmi et al., 2019; Holtzman et al., 2017; J. W. Hong et al., 2016; M. Hong et al., 2016; M. Iwasaki et al., 2021; T. Iwasaki et al., 2018; Jaafar et al., 2014; Jeong et al., 2020; Juarez et al., 2015; Jung et al., 2019, 2020; Khan et al., 2016; Kim et al., 2019; Konopka et al., 2015; Kwon et al., 2018; Lasta et al., 2019; Moya et al., 2014; Nakamura et al., 2020; Oliveira et al., 2021; Ortiz et al., 2018; Papapanou et al., 2020; Ra et al., 2020; Ramírez et al., 2017; Romero-Castro et al., 2020; Sakurai et al., 2021; Schmidt et al., 2020; Sekiguchi et al., 2020; Shariff et al., 2018; Shimizu et al., 2019; Shyagali et al., 2017; Silva-Junior et al., 2017, 2019; Sim et al., 2017; Singh et al., 2020; Skoskiewicz-Malinowska et al., 2018; E. Song et al., 2021; Y. H. Song et al., 2021; Stødle et al., 2021; Su et al., 2021; Suominen et al., 2018; Thanakun et al., 2014; Vano et al., 2015; Wahlin et al., 2018; Zaitsu et al., 2017; Zhao et al., 2019) were considered of moderate risk of bias while only twenty (Botelho et al., 2019; Cepeda et al., 2017; Clauss et al., 2021; Eke et al., 2015, 2018; Figueiredo et al., 2013; Ghassib et al., 2021; Ha et al., 2020; He et al., 2018; Holde et al., 2017; Jiao et al., 2021; Kotsakis et al., 2015; E. Lee & Lee, 2019; K. Lee & Kim, 2019; S.-W. Lee et al., 2017; Machado et al., 2021; Montero et al., 2019; Pinto-Filho et al., 2018; Shariff et al., 2017; Sun et al., 2020; Vallespir et al., 2014) were of low risk of bias (*Supplementary file 3*). Overall, studies failed to report prevalence data that represented closely the national population regarding relevant variables (62.5%, n=49) and to use an acceptable case definition of periodontitis (55.7%, n= 44). Non-response bias was minimal (75.1%, n= 61), while 61.7% (n=50) used some form of random selection, and 59.3% (n=48) studies had the prevalence period for the parameter of interest appropriate. The remaining items had predominantly low risk of bias. Figure 5 shows the Summary plot representing the risk of bias of the included studies (McGuinness & Higgins, 2021). Inter-examiner reliability at risk of bias assessment was rated as excellent (kappa score = 0.82, 95% CI: 0.79–0.84).

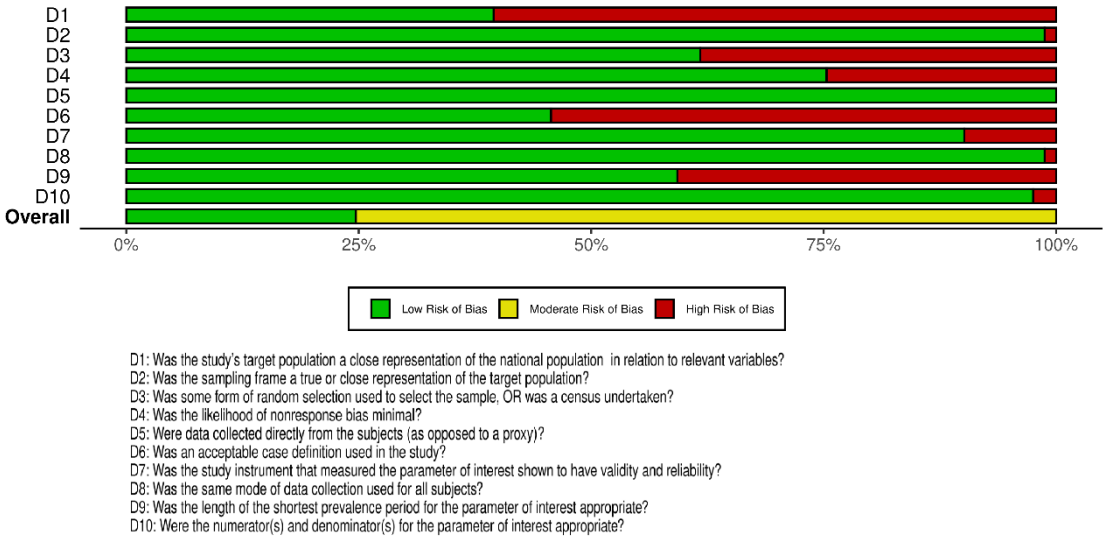


Figure 5 | ***Summary Plot of the Methodological quality of included studies***

4. POOLED ESTIMATES

Between 2011 and 2020, total of 25,637,885 adults were included in the overall pool of analyses, with 9,452,134 adults reported to have periodontitis. We started by comparing non-confident with confident case definitions of periodontitis. Overall, the results confirmed a significant difference ($p<0.00001$), with confident case definitions (62.5%, 95% CI: 56.9-67.8, $p<0.000001$, $I^2=99.2\%$) reporting nearly twice the prevalence than non-confident classifications (37.0%, 95% CI: 30.8-44.5, $I^2=99.7\%$). For this reason, and following the instruction of GRADE, we focused on the estimates using confident periodontal case definitions (Schünemann et al., 2008).

Furthermore, we explored the impact of partial-mouth protocols and non-reported protocols in the overall estimates. Sensitivity analyses showed that studies using a full-mouth protocol reported nearly twice the prevalence (59.1%, 95% CI: 53.0-65.0, $p<0.000001$, $I^2=99.7\%$, number of studies = 44), that partial-mouth protocols (30.1%, 95% CI: 24.4-36.0, $p<0.000001$, I2=99.6%, number of studies = 33), or not-reported protocols (58.4%, 95% CI: 41.0-74.7, $p<0.000001$, $I^2=98.3\%$, number of studies = 3). The comparison for subgroup differences was significant ($p<0.0001$).

4.1. Total Prevalence

The overall prevalence of periodontitis was estimated at 62.5% (95% CI: 52.7-67.0, $p<0.000001$, $I^2=99.32\%$), comprising eighteen different countries. This estimate was confirmed not to be affected by the methodological quality ($p=0.30181651$), comparing

studies of low risk of bias (58.1%, 95% CI: 51.2-64.9, p<0.000001, I^2=99.23%) than studies with moderate risk of bias (65.6%, 95% CI: 57.5-73.2, p<0.000001, I^2=99.0%). Heterogeneity was considered to be substantial.

The latitude (estimate=0.001, SE=0.002, p=0.586), the longitude (estimate=0.000, SE=0.001, p=0.739) and sample size (estimate=0.000, SE=0.000, p=0.805) were confirmed to have no influence on the final estimates, through meta-regression. In addition, no publication bias was detected (Egger test=1.75, SE=3.55, p=0.625).

Considering the case definition, there were significant differences between all four reported classifications (p=0.0005) (Table 2). Estimates reporting using CDC/AAP (2012) case definition presented the highest estimate (68.0%) while estimates using the CDC/AAP 2007 presented the lowest (49.3%).

We further analyzed whether the age interval of participants in the included studies would influence the results. Overall, the test for subgroup differences confirmed a significant difference according to the age intervals defined in the studies (p=0.0132). Studies reporting prevalence data of elderly participants (≥65 years old or older) with a 79.4% overall percentage (95% CI: 68.9-88.1, p<0.000001, I^2=96.3%).

4.2. Prevalence per Continent

Considering the geographic location, the pooled estimate from the European continent was the highest (65.5%), while the South American continent had the lowest (54.9%) (Table 2). Yet, all continents reported significantly pooled estimates exceeding 50%.

4.3. Severity

In what severity concerns (Table 3), the pooled measures pointed to an estimated moderate-to-severe periodontitis prevalence of 54.8% (95% CI: 47.1-62.3, p<0.000001, I2=99.2%). Although with substantial heterogeneity, this estimate was relatively stable and not influenced by female/male ratio (-0.198, p=0.3442), latitude (0.002, p=0.6145), longitude (0.000, p=0.8788) or sample size (-0.000, p=0.8358). The estimated prevalence of severe periodontitis was 24.2% (95% CI: 18.1-30.7, p<0.000001, I2=99.6%). Similarly, we observed high heterogeneity and this estimate was significantly influenced by the male/female ratio (-0.393, p=0.0224), but not by other variables.

Table 2 │ ***Periodontitis prevalence according to the type of confident case definition.***

	n	PP	95% CI	T	T^2	I^2 (%)	p-value	Egger test [SE] (p-value)
Overall	31	62.5	56.9-67.8	0.16	0.03	99.1	<0.000001	1.75 [3.554] (0.625)
Risk of Bias								
Low	13	58.1	51.2-64.9	0.13	0.02	99.3	<0.000001	1.82 [6.82] (0.794)
Moderate	18	65.6	57.5-73.2	0.18	0.03	99.0	<0.000001	-3.29 [5.49] (0.558)
Case Definition								
EFP/AAP (2018)	6	52.3	38.2-66.2	0.18	0.03	99.4	<0.000001	-
CDC/AAP (2012)	18	68.0	61.3-74.2	0.15	0.02	99.4	<0.000001	13.91 [4.74] (0.010)
CDC/AAP (2007)	4	49.3	41.4-57.2	0.08	0.01	92.6	<0.000001	-
AAP (1999)	3	66.7	61.3-71.8	0.04	0.00	50.5	<0.000001	-
Age Interval								
Wider age interval (≥18/≥19)	12	57.1	46.9-67.0	0.18	0.03	99.3	<0.000001	-4.56 [6.81] (0.519)
≥30 years old	11	62.7	55.2-69.8	0.13	0.02	99.3	<0.000001	4.79 [6.78] (0.498)
≥40 years old	2	60.1	58.3-61.8	0.00	0.00	0.0	<0.000001	-
<65 years old	2	59.4	34.5-81.9	0.18	0.03	98.7	<0.000001	-
≥65 years old	4	79.4	68.9-88.1	0.12	0.01	96.3	<0.000001	-
Continent								
Asia	11	64.3	55.8-72.4	0.15	0.02	99.5	<0.000001	-0.91 [3.16] (0.780)
Europe	5	65.5	48.7-80.5	0.19	0.04	99.5	<0.000001	-
North America	10	62.4	55.0-69.5	0.12	0.01	97.6	<0.000001	17.73 [7.49] (0.070)
South America	5	54.9	33.4-75.5	0.06	0.25	99.4	<0.000001	-

CI –Confidence Interval; PP – Pooled Prevalence ; I^2– I squared; n – Number of studies; T – tau; T^2 – tau squared

4.4. Additional Analysis

When inspecting the existence of publication bias, funnel asymmetry was only found at studies reporting periodontitis using the CDC/AAP (2012) (estimate=13.9110.93, SE=4.744.94, p=0.00142) (Table 2). For the remaining estimates, no publication bias was observed.

Table 3 | ***Periodontitis prevalence according to the form of periodontitis.***

Periodontitis	n	PP	95% CI	T	T^2	I^2 (%)	p-value	Egger test [SE] (p-value)
Moderate-to-Severe vs. Mild-No	25	54.8	47.1-62.3	0.19	0.04	99.2	<0.000001	3.25 [4.40] (0.468)
Severe vs. non-Severe	24	24.2	18.1-30.7	0.18	0.03	99.6	<0.000001	2.06 [5.81] (0.7260)

IV. DISCUSSION

1. SUMMARY OF THE MAIN RESULTS

The main aim of the present systematic review was to estimate the prevalence of periodontitis reported in studies between 2011 and 2020, and as a secondary objective to evaluate the prevalence geographically, to compare confident and non-confident case definitions, and other confounding variables. Accordingly, the findings of this systematic confirm that periodontitis continues to be a serious global public health issue, with a pooled prevalence of approximately 63% from studies conducted between 2011 and 2020. Moderate-to-severe cases pooled prevalence was 54.8% while severe periodontitis was 24.2%.

Furthermore, the use of non-confident classifications when reporting the periodontal outcomes, leads to an underestimation of almost 50% (37.0%), when compared with confident case definitions (62.5%). Therefore, we focused solely on the estimates reported through confident case definitions, which comprised seventeen different countries. Regarding confident classifications, there were also significant differences. The CDC/AAP 2012 was the most employed diagnostic criteria and with the highest estimate (68.0%), while the EFP/AAP 2018 case definition estimated a prevalence of 52,3%.

2. EVIDENCE QUALITY AND POTENTIAL BIAS IN THE REVIEW PROCESS

This systematic review strengths and limitations are mostly related to the methodological quality of the included studies per se, while this study was prepared and reported according to state-of-the-art guidelines and had a comprehensive analysis on possible confounding variables that could affect the results. Indeed, prevalence was strictly affected by periodontal case definitions regarding their confidence. As for the remaining variables they were not influential on the final estimates. Defining the confidence of a case definition always implies an uncertain degree of selection bias, yet this decision was based on a previous study by Muñoz-Aguilera that found significant weight on the results (Muñoz Aguilera et al., 2020). Similarly, studies with confident

case definitions reported almost twice the prevalence than those using non-confident classifications in the present results.

Still in the periodontal case definitions, our meta-analytical estimates differ from previous studies using GBD approach (Chen et al., 2021; Kassebaum et al., 2014; Marcenes et al., 2013; Wu et al., 2022). On the one hand, GBD estimates arise from complex and strong iterative approaches and thus provide worldwide approximations, yet with some sort of underestimation due to the use of less reliable diagnostic criteria (such as the Community Periodontal Index [CPI] or the CPI of Treatment Needs) (GBD, 2015). On the other hand, our approach provides more reliable estimations based on full-mouth examinations and diagnostic consensus, nevertheless, the existence of several confident case definitions confuses the comparison among studies. Consequently, implementing a consensus to strengthening the surveillance of periodontitis will certainly benefit Periodontal Research and future meta-epidemiological studies. Defining mandatory periodontal clinical measures (such as PPD and CAL) and thresholds, and providing results for at least two diagnostic criteria (CDC/AAP 2012 and EFP/AAP 2018) are suggestions that may contribute to the robustness of periodontal prevalence reporting. Yet, narrowing the results according to the case definition confidence may have certainly resulted in less geographic coverage and was contingent to available epidemiological studies.

Finally, several studies were lacking information on male/female prevalence ration, clear age intervals, distribution according to smoking habits, socioeconomic data, and distribution of periodontitis according to its severity. Thus, our examination on additional sources of heterogeneity and interpretation of the results was restricted and could be expanded in the future if studies provide such information.

3. AGREEMENTS AND DISAGREEMENTS WITH OTHER REVIEWS OR STUDIES

There is an overall agreement the prevalence and incidence of periodontitis have been increasing, possibly due to population growth and aging (Bernabe et al., 2020; Kassebaum et al., 2017; Marcenes et al., 2013; Peres et al., 2019; Watt et al., 2019; Wu et al., 2022). These results align with this consensus and highlights the need for better periodontal care programs mainly focusing the poor and socially-disadvantaged populations that are disproportionally affected.

In Wu et al. (Wu et al., 2022), GBD data allowed to assess all regions and countries which was not possible to achieve with our estimates. In the latter, periodontitis was mostly prevalent between 55-59 years old and with substantial prevalence from 55 onwards. Similarly, our age subgroup meta-analysis showed individuals with 65 years old or older to have the highest prevalence when compared with younger age groups. Regarding severe periodontitis, our results reported a substantial prevalence of severe periodontitis (24.2%), and a possibly increasing when compared to the outputs from Kassebaum et al. (Kassebaum et al., 2014), a global prevalence of 11.2%. Although the methodologies between these estimates differ, and for this reason some estimation discrepancy may exist, our estimates uphold a recent forecast that severe periodontitis could increase (Kassebaum et al., 2014).

The findings from this study can inform global health stakeholders about the prevalence of periodontitis from epidemiological studies to preempt and better manage public periodontal health strategies. However, due to the limited number of countries represented in the final sample, the generalizability of these estimates is limited. Therefore, we urge for the need for continuing epidemiological surveillance, from both national and regional settings, using appropriate diagnostic strategies, to better convey accurate estimates and to allow meta-analytical global outputs.

V. CONCLUSION

According to this systematic review, it can be stated that throughout the last decade (from 2011 to 2020), the cumulative prevalence of periodontitis was estimated to be close to 60%, with its severe stage affecting almost 25% of the population.

When compared to the estimates from previous studies, these outcomes exhibit important clinical relevance, due to the persistently high prevalence of periodontitis worldwide.

VI. FUTURE PERSPECTIVES

The results of this systematic review ensure that the periodontitis prevalence and incidence exhibit an enduring high prevalence, and lately have been rising, presumably as a result of population growth and aging. Therefore, putting into practice a consensus to improve the surveillance of periodontitis will undoubtedly help Periodontal Research and future meta-epidemiological investigations. To increase the reliability of periodontal prevalence reporting, it is suggested that mandatory periodontal clinical assessments (such PPD, CAL, PISA, or PESA) and thresholds be established, as well as results for at least two diagnostic criteria (CDC/AAP 2012 and EFP/AAP 2018).

The access to the current trends of periodontitis allows for better planning of dental services and workforce, providing better periodontal care programs that prioritize the impoverished and socially disadvantaged individuals that are disproportionately affected.

VII. BIBLIOGRAPHY

Alqaderi, H., Goodson, J. M., & Agaku, I. (2020). Association between sleep and severe periodontitis in a nationally representative adult US population. *Journal of Periodontology*, *91*(6), 767–774. https://doi.org/10.1002/JPER.19-0105

ARCPOH. (2019). *AUSTRALIA ' S ORAL HEALTH National Study of Adult Oral Health 2017-18*.

Armitage, G. C. (1999). Development of a classification system for periodontal diseases and conditions. *Annals of Periodontology / the American Academy of Periodontology*, *4*(1), 1–6. https://doi.org/10.1902/annals.1999.4.1.1

Balaji, S., Lavu, V., & Rao, S. (2018). Chronic periodontitis prevalence and the inflammatory burden in a sample population from South India. *Indian Journal of Dental Research*, *29*(2), 254–259. https://doi.org/10.4103/ijdr.IJDR_335_17

Barendregt, J. J., Doi, S. A., Lee, Y. Y., Norman, R. E., & Vos, T. (2013). Meta-analysis of prevalence. *Journal of Epidemiology and Community Health*, *67*(11), 974–978. https://doi.org/10.1136/jech-2013-203104

Belbasis, L., & Bellou, V. (2018). Introduction to Epidemiological Studies. Genetic Epidemiology. *An Automated Irrigation System Using Arduino Microcontroller*, *1793*(January), 1–6. https://doi.org/10.1007/978-1-4939-7868-7

Beltrán-Aguilar, E. D., Eke, P. I., Thornton-Evans, G., & Petersen, P. E. (2012). Recording and surveillance systems for periodontal diseases. *Periodontology 2000*, *60*(1), 40–53. https://doi.org/10.1111/j.1600-0757.2012.00446.x

Bernabe, E., Marcenes, W., Hernandez, C. R., Bailey, J., Abreu, L. G., Alipour, V., Amini, S., Arabloo, J., Arefi, Z., Arora, A., Ayanore, M. A., Bärnighausen, T. W., Bijani, A., Cho, D. Y., Chu, D. T., Crowe, C. S., Demoz, G. T., Demsie, D. G., Dibaji Forooshani, Z. S., … Kassebaum, N. J. (2020). Global, Regional, and National Levels and Trends in Burden of Oral Conditions from 1990 to 2017: A Systematic Analysis for the Global Burden of Disease 2017 Study. *Journal of Dental Research*, *99*(4), 362–373. https://doi.org/10.1177/0022034520908533

Bhat, M., Do, L. G., & Roberts-Thomson, K. (2018). Risk indicators for prevalence, extent and severity of periodontitis among rural Indian population aged 35-54 years. *International Journal of Dental Hygiene*, *16*(4), 492–502. https://doi.org/10.1111/idh.12351

Bhat, M., Roberts-Thomson, K., & Do, L. G. (2015). Clustering of risk indicators for

periodontal disease: A population-based study. *Community Dental Health*, *32*(3), 158–162. https://doi.org/10.1922/CDH_3569Bhat05

Bilgin Çetin, M., Sezgin, Y., Maraş, E., & Cebeci, İ. A. (2021). Association of probable bruxism with periodontal status: A cross-sectional study in patients seeking periodontal care. *Journal of Periodontal Research*, *56*(2), 370–378. https://doi.org/10.1111/jre.12829

Bongo, A. K. S., Brustad, M., Oscarson, N., & Jönsson, B. (2021). Periodontal health in an indigenous Sámi population in Northern Norway: a cross-sectional study. *BMC Oral Health*, *21*(1), 334. https://doi.org/10.1186/s12903-021-01631-y

Borgnakke, W. S. (2015). Does Treatment of Periodontal Disease Influence Systemic Disease? *Dental Clinics of North America*, *59*(4), 885–917. https://doi.org/10.1016/j.cden.2015.06.007

Botelho, J., Machado, V., Leira, Y., Proença, L., Chambrone, L., & Mendes, J. J. (2021). Economic burden of periodontitis in the United States and Europe – an updated estimation. *Journal of Periodontology*, *February*, 1–7. https://doi.org/10.1002/JPER.21-0111

Botelho, J., Machado, V., Proença, L., Alves, R., Cavacas, M. A., Amaro, L., & Mendes, J. J. (2019). Study of Periodontal Health in Almada-Seixal (SoPHiAS): a cross-sectional study in the Lisbon Metropolitan Area. *Scientific Reports*, *9*(1), 1–10. https://doi.org/10.1038/s41598-019-52116-6

Botelho, J., Machado, V., Proença, L., & Mendes, J. J. (2020). The 2018 periodontitis case definition improves accuracy performance of full-mouth partial diagnostic protocols. *Scientific Reports*, *10*(1), 1–7. https://doi.org/10.1038/s41598-020-63700-6

Bouchard, P., Carra, M. C., Boillot, A., Mora, F., & Rangé, H. (2017). Risk factors in periodontology: a conceptual framework. *Journal of Clinical Periodontology*, *44*(2), 125–131. https://doi.org/10.1111/jcpe.12650

Burt, B. (2005). Position Paper: Epidemiology of Periodontal Diseases. *Journal of Periodontology*, *76*(8), 1406–1419. https://doi.org/10.1902/jop.2005.76.8.1406

Buset, S. L., Walter, C., Friedmann, A., Weiger, R., Borgnakke, W. S., & Zitzmann, N. U. (2016). Are periodontal diseases really silent? A systematic review of their effect on quality of life. *Journal of Clinical Periodontology*, *43*(4), 333–344. https://doi.org/10.1111/jcpe.12517

Castrejón-Pérez, R. C., Jiménez-Corona, A., Bernabé, E., Villa-Romero, A. R., Arrivé,

E., Dartigues, J. F., Gutiérrez-Robledo, L. M., & Borges-Yáñez, S. A. (2017). Oral Disease and 3-Year Incidence of Frailty in Mexican Older Adults. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, *72*(7), 951–957. https://doi.org/10.1093/gerona/glw201

Caton, J. G., Armitage, G., Berglundh, T., Chapple, I. L. C., Jepsen, S., Kornman, K. S., Mealey, B. L., Papapanou, P. N., Sanz, M., & Tonetti, M. S. (2018). A new classification scheme for periodontal and peri-implant diseases and conditions – Introduction and key changes from the 1999 classification. *Journal of Periodontology*, *89*(S1), S1–S8. https://doi.org/10.1002/JPER.18-0157

Cepeda, M. S., Weinstein, R., Blacketer, C., & Lynch, M. C. (2017). Association of flossing/inter-dental cleaning and periodontitis in adults. *Journal of Clinical Periodontology*, *44*(9), 866–871. https://doi.org/10.1111/jcpe.12765

Chambrone, L., Foz, A. M., Guglielmetti, M. R., Pannuti, C. M., Artese, H. P. C., Feres, M., & Romito, G. A. (2013). Periodontitis and chronic kidney disease: A systematic review of the association of diseases and the effect of periodontal treatment on estimated glomerular filtration rate. *Journal of Clinical Periodontology*, *40*(5), 443–456. https://doi.org/10.1111/jcpe.12067

Chapple, I. L. C., & Genco, R. (2013). Diabetes and periodontal diseases: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *Journal of Periodontology*, *84*(4-s), S106–S112. https://doi.org/10.1902/jop.2013.1340011

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. https://doi.org/10.1111/jcpe.13506

Clauss, A., Sie, A., Zabre, P., Schmoll, J., Sauerborn, R., & Listl, S. (2021). Population-Based Prevalence of Oral Conditions as a Basis for Planning Community-Based Interventions: An Epidemiological Study From Rural Burkina Faso. *Frontiers in Public Health*, *9*(July), 1–9. https://doi.org/10.3389/fpubh.2021.697498

Costa, F. O., Guimarães, A. N., Cota, L. O. M., Pataro, A. L., Segundo, T. K., Cortelli, S. C., & Costa, J. E. (2009). Impact of different periodontitis case definitions on periodontal research. *Journal of Oral Science*, *51*(2), 199–206. https://doi.org/10.2334/josnusd.51.199

Costa, P. D., Canaan, J. C. R., Castelo, P. M., Fonseca, D. C., Pereira- Dourado, S. M.,

Murata, R. M., Pardi, V., & Pereira, L. J. (2021). Influence of Micronutrient Intake, Sociodemographic, and Behavioral Factors on Periodontal Status of Adults Assisted by a Public Health Care System in Brazil: A Cross-Sectional Multivariate Analysis. *Nutrients*, *13*, 973.

Darveau, R. P. (2010). Periodontitis: A polymicrobial disruption of host homeostasis. *Nature Reviews Microbiology*, *8*(7), 481–490. https://doi.org/10.1038/nrmicro2337

Dhaifullah, E., Al-Maweri, S. A., Koppolu, P., Elkhtat, E., Mostafa, D., & Mahgoub, M. (2019). Body mass index and periodontal health status among young Saudi adults: A cross-sectional study. *Annals of Saudi Medicine*, *39*(6), 433–440. https://doi.org/10.5144/0256-4947.2019.433

Díaz-Reissner, C., Roldán-Merino, J., & García, I. C. (2020). Association between self-assessment and clinical oral health status in adults, Paraguay. *Journal of Oral Research*, *9*(6), 483–489. https://doi.org/10.17126/joralres.2020.094

Donos, N. (2018). The periodontal pocket. *Periodontology 2000*, *76*(1), 7–15. https://doi.org/10.1111/prd.12203

Dumitrescu, A. L. (2016). Editorial: Periodontal Disease - A Public Health Problem. *Frontiers in Public Health*, *3*, 278. https://doi.org/10.1111/idj.12185

Dye, B. A. (2012). Global periodontal disease epidemiology. *Periodontology 2000*, *58*(1), 10–25. https://doi.org/10.1111/j.1600-0757.2011.00413.x

Ebersole, J. L. (2003). Humoral immune responses in gingival crevice fluid: Local and systemic implications. *Periodontology 2000*, *31*(Table 2), 135–166. https://doi.org/10.1034/j.1600-0757.2003.03109.x

Eke, P., Dye, B. A., Wei, L., Slade, G. D., Thornton-Evans, G. O., Borgnakke, W. S., Taylor, G. W., Page, R. C., Beck, J. D., & Genco, R. J. (2015). Update on Prevalence of Periodontitis in Adults in the United States: NHANES 2009 to 2012. *Journal of Periodontology*, *86*(5), 611–622. https://doi.org/10.1902/jop.2015.140520

Eke, P., Dye, B. A., Wei, L., Thornton-Evans, G. O., & Genco, R. J. (2012). Prevalence of periodontitis in adults in the united states: 2009 and 2010. *Journal of Dental Research*, *91*(10), 914–920. https://doi.org/10.1177/0022034512457373

Eke, P., Page, R. C., Wei, L., Thornton-Evans, G., & Genco, R. J. (2012). Update of the Case Definitions for Population-Based Surveillance of Periodontitis Paul. *J Periodontol.*, *83*(12), 1449–1454. https://doi.org/doi:10.1902/jop.2012.110664

Eke, P., Thornton-Evans, G. O., Wei, L., Borgnakke, W. S., Dye, B. A., & Genco, R. J.

(2018). Periodontitis in US Adults: National Health and Nutrition Examination Survey 2009–2014. *Journal of the American Dental Association*, *149*(7), 576–588. https://doi.org/10.1016/j.adaj.2018.04.023.Periodontitis

Figueiredo, A., Soares, S., Lopes, H., Dos Santos, J. N., Ramalho, L. M. P., Cangussu, M. C., & Cury, P. R. (2013). Destructive periodontal disease in adult Indians from Northeast Brazil: Cross-sectional study of prevalence and risk indicators. *Journal of Clinical Periodontology*, *40*(11), 1001–1006. https://doi.org/10.1111/jcpe.12147

Fischer, R. G., Junior, L., R., R.-V., B., F., L. C., M., Z., S., & Feres, M. (2020). Periodontal disease and its impact on general health in Latin America. Section V: Treatment of periodontitis. *Brazilian Oral Research*, *34*(supp1 1), e026. https://doi.org/10.1590/1807-3107BOR-2020.VOL34.0024

GBD. (2015). *Protocol for the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD)*. *March*, 1–29. http://www.healthdata.org/sites/default/files/files/Projects/GBD/GBD_Protocol.pdf

Genco, R. J., & Borgnakke, W. S. (2013). Risk factors for periodontal disease. *Periodontology 2000*, *62*(1), 59–94. https://doi.org/10.1111/j.1600-0757.2012.00457.x

Germen, M., Baser, U., Lacin, C. C., Fıratlı, E., İşsever, H., & Yalcin, F. (2021). Periodontitis prevalence, severity and risk factors: A comparison of the aap/cdc case definition and the efp/aap classification. *International Journal of Environmental Research and Public Health*, *18*(7). https://doi.org/10.3390/ijerph18073459

Ghassib, I. H., Batarseh, F. A., Wang, H. L., & Borgnakke, W. S. (2021). Clustering by periodontitis-associated factors: A novel application to NHANES data. *Journal of Periodontology*, *92*(8), 1136–1150. https://doi.org/10.1002/JPER.20-0489

Giacaman, R. A., Sandoval Salas, D., Bustos Alvarez, I. P., Rojas Cáceres, M. A., & Mariño, R. J. (2016). Epidemiología del estado de salud periodontal en la VII Región del Maule, Chile. *Revista Clínica de Periodoncia, Implantología y Rehabilitación Oral*, *9*(2), 184–192. https://doi.org/10.1016/j.piro.2016.07.002

Goel, K., Sharma, S., Baral, D. D., & Agrawal, S. K. (2021). Current status of periodontitis and its association with tobacco use amongst adult population of Sunsari district, in Nepal. *BMC Oral Health*, *21*(1), 1–9. https://doi.org/10.1186/s12903-021-01416-3

Gomes-Filho, I. S., Santos, P. N. P., Cruz, S. S., Figueiredo, A. C. M. G., Trindade, S.

C., Ladeia, A. M., Cerqueira, E. M. M., Passos-Soares, J. S., Coelho, J. M. F., Hintz, A. M., Barreto, M. L., Fischer, R. G., Loomer, P. M., & Scannapieco, F. A. (2021). Periodontitis and its higher levels of severity are associated with the triglyceride/high density lipoprotein cholesterol ratio. *Journal of Periodontology*, *92*(11), 1509–1521. https://doi.org/10.1002/JPER.21-0004

Graziani, F., Gennai, S., Solini, A., & Petrini, M. (2018). A systematic review and meta-analysis of epidemiologic observational evidence on the effect of periodontitis on diabetes An update of the EFP-AAP review. *Journal of Clinical Periodontology*, *45*(2), 167–187. https://doi.org/10.1111/jcpe.12837

Ha, D. H., John Spencer, A., Ju, X., & Do, L. G. (2020). Periodontal diseases in the Australian adult population. *Australian Dental Journal*, *65*(S1), S52–S58. https://doi.org/10.1111/adj.12765

Haag, D. G., Peres, K. G., Balasubramanian, M., & Brennan, D. S. (2017). Oral Conditions and Health-Related Quality of Life: A Systematic Review. *Journal of Dental Research*, *96*(8), 864–874. https://doi.org/10.1177/0022034517709737

Hajishengallis, G. (2015). Periodontitis: From microbial immune subversion to systemic inflammation. *Nature Reviews Immunology*, *15*(1), 30–44. https://doi.org/10.1038/nri3785

Han, D. H., & Kim, M. S. (2021). Are occupational and environmental noises associated with periodontitis? Evidence from a Korean representative cross-sectional study. *BMC Public Health*, *21*(1), 1–9. https://doi.org/10.1186/s12889-021-10672-5

Han, K., & Park, J. B. (2017). Underweight is associated with periodontitis among Korean female adults. *Biomedical Research (India)*, *28*(12), 5609–5614.

Han, S. J., Bae, K. H., Lee, H. J., Kim, S. J., & Cho, H. J. (2019). Association between regular walking and periodontitis according to socioeconomic status: a cross-sectional study. *Scientific Reports*, *9*(1), 1–8. https://doi.org/10.1038/s41598-019-49505-2

He, S., Wei, S., Wang, J., & Ji, P. (2018). Chronic periodontitis and oral health-related quality of life in chinese adults: A population-based, cross-sectional study. *Journal of Periodontology*, *89*(3), 275–284. https://doi.org/10.1002/JPER.16-0752

Helmi, M. F., Huang, H., Goodson, J. M., Hasturk, H., Tavares, M., & Natto, Z. S. (2019). Prevalence of periodontitis and alveolar bone loss in a patient population at Harvard School of Dental Medicine. *BMC Oral Health*, *19*(1), 1–11.

https://doi.org/10.1186/s12903-019-0925-z

Higgins, J. P. T., Thomas, J., Chandlers, J., Cumpston, M., Li, T., Page, M. J., & Welch, V. A. (2019). *Cochrane Handbook for Systematic Reviews of Interventions* (2nd ed.). John Wiley & Sons.

Holde, G. E., Oscarson, N., Trovik, T. A., Tillberg, A., & Jönsson, B. (2017). Periodontitis Prevalence and Severity in Adults: A Cross-Sectional Study in Norwegian Circumpolar Communities. *Journal of Periodontology*, *88*(10), 1012–1022. https://doi.org/10.1902/jop.2017.170164

Holtfreter, B., Albandar, J. M., Dietrich, T., Dye, B. A., Eaton, K. A., Eke, P. I., Papapanou, P. N., & Kocher, T. (2015). Standards for reporting chronic periodontitis prevalence and severity in epidemiologic studies: Proposed standards from the Joint EU/USA Periodontal Epidemiology Working Group. *Journal of Clinical Periodontology*, *42*(5), 407–412. https://doi.org/10.1111/jcpe.12392

Holtzman, J. S., Atchison, K. A., Macek, M. D., & Markovic, D. (2017). Oral Health Literacy and Measures of Periodontal Disease. *Journal of Periodontology*, *88*(1), 78–88. https://doi.org/10.1902/jop.2016.160203.Oral

Hong, J. W., Noh, J. H., & Kim, D. J. (2016). The Prevalence and Associated Factors of Periodontitis According to Fasting Plasma Glucose in the Korean Adults. *Medicine (United States)*, *95*(14), 1–8. https://doi.org/10.1097/MD.0000000000003226

Hong, M., Kim, H. Y., Seok, H., Yeo, C. D., Kim, Y. S., Song, J. Y., Lee, Y. B., Lee, D. H., Lee, J. I., Lee, T. K., Ahn, H. S., Ko, Y. H., Jeong, S. C., Chae, H. S., & Sohn, T. S. (2016). Prevalence and risk factors of periodontitis among adults with or without diabetes mellitus. *Korean Journal of Internal Medicine*, *31*(5), 910–919. https://doi.org/10.3904/kjim.2016.031

Hoy, D., Brooks, P., Woolf, A., Blyth, F., March, L., Bain, C., Baker, P., Smith, E., & Buchbinder, R. (2012). Assessing risk of bias in prevalence studies: Modification of an existing tool and evidence of interrater agreement. *Journal of Clinical Epidemiology*, *65*(9), 934–939. https://doi.org/10.1016/j.jclinepi.2011.11.014

Humagain, M., & Adhikari, S. (2018). Assessment of periodontal status of the people in chepang hill tract of Nepal: A cross sectional study. *Kathmandu University Medical Journal*, *16*(63), 206–210.

Humphrey, L. L., Fu, R., Buckley, D. I., Freeman, M., & Helfand, M. (2008). Periodontal disease and coronary heart disease incidence: A systematic review and meta-analysis. *Journal of General Internal Medicine*, *23*(12), 2079–2086.

https://doi.org/10.1007/s11606-008-0787-6

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). https://doi.org/10.1111/jcpe.12063

Iwasaki, M., Usui, M., Ariyoshi, W., Nakashima, K., Nagai-Yoshioka, Y., Inoue, M., Kobayashi, K., & Nishihara, T. (2021). Interruption of regular dental visits during the COVID-19 pandemic due to concerns regarding dental visits was associated with periodontitis in Japanese office workers. *Journal of Periodontal Research*, *56*(6), 1091–1098. https://doi.org/10.1111/jre.12923

Iwasaki, T., Hirose, A., Azuma, T., Ohashi, T., Watanabe, K., Obora, A., Deguchi, F., Kojima, T., Isozaki, A., & Tomofuji, T. (2018). Correlation between ultrasound-diagnosed non-alcoholic fatty liver and periodontal condition in a cross-sectional study in Japan. *Scientific Reports*, *8*(1), 1–7. https://doi.org/10.1038/s41598-018-25857-z

Jaafar, N., Hakim, H., Mohd Nor, N. A., Mohamed, A., Saub, R., Esa, R., Doss, J., Mohd Yusof, Z. Y., Ab-Murat, N., Abu Kassim, N. L., & Majid, H. A. (2014). Is the burden of oral diseases higher in urban disadvantaged community compared to the national prevalence? *BMC Public Health*, *14*(Suppl 3), S2. https://doi.org/10.1186/1471-2458-14-S3-S2

Jeong, W., Choi, D.-W., Kim, Y. K., Lee, H. J., Lee, S. A., Park, E.-C., & Jang, S.-I. (2020). Associations of Electronic and Conventional Cigarette Use with Periodontal Disease in South Korean Adults. *Journal of Periodontology*, *91*(1), 55–64. https://doi.org/10.1902/jper.10397.This

Jiao, J., Jing, W., Si, Y., Feng, X., Tai, B., Hu, D., Lin, H., Wang, B., Wang, C., Zheng, S., Liu, X., Rong, W., Wang, W., Li, W., Meng, H., & Wang, X. (2021). The prevalence and severity of periodontal disease in Mainland China: Data from the Fourth National Oral Health Survey (2015-2016). *Journal of Clinical Periodontology*, *48*(2), 168–179. https://doi.org/10.1111/jcpe.13396

Juarez, I., Hernández, M., Letelier, C., Halabí, D., & Araneda, C. (2015). Association between abdominal obesity and periodontal disease. Cross-sectional study. *Journal Oral Of Research*, *4*(2), 95–102. https://doi.org/10.17126/joralres.2015.021

Jung, E. S., Choi, Y. Y., & Lee, K. H. (2019). Relationship between rheumatoid arthritis and periodontal disease in Korean adults: Data from the Sixth Korea National Health and Nutrition Examination Survey, 2013 to 2015. *Journal of*

Periodontology, *90*(4), 350–357. https://doi.org/10.1002/JPER.18-0290

Jung, E. S., Lee, K. H., & Choi, Y. Y. (2020). Association between oral health status and chronic obstructive pulmonary disease in Korean adults. *International Dental Journal*, *70*(3), 208–213. https://doi.org/10.1111/idj.12535

Kassebaum, N. J., Bernabé, E., Dahiya, M., Bhandari, B., Murray, C. J. L., & Marcenes, W. (2014). Global burden of severe periodontitis in 1990-2010: A systematic review and meta-regression. *Journal of Dental Research*, *93*(11), 1045–1053. https://doi.org/10.1177/0022034514552491

Kassebaum, N. J., Smith, A. G. C., Bernabé, E., Fleming, T. D., Reynolds, A. E., Vos, T., Murray, C. J. L., Marcenes, W., Abyu, G. Y., Alsharif, U., Asayesh, H., Benzian, H., Dandona, L., Dandona, R., Kasaeian, A., Khader, Y. S., Khang, Y. H., Kokubo, Y., Kotsakis, G. A., … Yonemoto, N. (2017). Global, Regional, and National Prevalence, Incidence, and Disability-Adjusted Life Years for Oral Conditions for 195 Countries, 1990-2015: A Systematic Analysis for the Global Burden of Diseases, Injuries, and Risk Factors. *Journal of Dental Research*, *96*(4), 380–387. https://doi.org/10.1177/0022034517693566

Keller, A., Rohde, J. F., Raymond, K., & Heitmann, B. L. (2015). Association Between Periodontal Disease and Overweight and Obesity: A Systematic Review. *Journal of Periodontology*, *86*(6), 766–776. https://doi.org/10.1902/jop.2015.140589

Khan, S., Khalid, T., & Awan, K. H. (2016). Chronic periodontitis and smoking: Prevalence and dose-response relationship. *Saudi Medical Journal*, *37*(8), 889–894. https://doi.org/10.15537/smj.2016.8.14223

Kim, J. S., Kim, S. Y., Byon, M. J., Lee, J. H., Jeong, S. H., & Kim, J. B. (2019). Association between periodontitis and metabolic syndrome in a korean nationally representative sample of adults aged 35–79 years. *International Journal of Environmental Research and Public Health*, *16*(16), 1–11. https://doi.org/10.3390/ijerph16162930

Kinane, D. F., Stathopoulou, P. G., & Papapanou, P. N. (2017). Periodontal diseases. *Nature Reviews Disease Primers*, *3*, 1–14. https://doi.org/10.1038/nrdp.2017.38

Kingman, A., Susin, C., & Albandar, J. M. (2008). Effect of partial recording protocols on severity estimates of periodontal disease. *Journal of Clinical Periodontology*, *35*(8), 659–667. https://doi.org/10.1111/j.1600-051X.2008.01243.x

Konopka, T., Dembowska, E., Pietruska, M., Dymalski, P., & Górska, R. (2015). Periodontal status and selected parameters of oral condition of Poles aged 65 to 74

years. *Przegląd Epidemiologiczny*, *69*(3).

Kotsakis, G. A., Thai, A., Ioannou, A. L., Demmer, R. T., & Michalowicz, B. S. (2015). Association between low-dose aspirin and periodontal disease: Results from the continuous national health and nutrition examination survey (NHANES) 2011-2012. *Journal of Clinical Periodontology*, *42*(4), 333–341. https://doi.org/10.1111/jcpe.12380

Kwon, Y. J., Park, J. W., Lim, H. J., Lee, Y. J., Lee, H. S., & Shim, J. Y. (2018). Triglyceride to high density lipoprotein cholesterol ratio and its association with periodontal disease in Korean adults: findings based on the 2012–2014 Korean national health and nutrition examination survey. *Clinical Oral Investigations*, *22*(1), 515–522. https://doi.org/10.1007/s00784-017-2140-0

Lasta, R., Devilla, A., Simoni, V., Foralosso, J. C., Kellermann, M. G., Marcon, S., Corralo, V. da S., & Rodrigues-Junior, S. A. (2019). Oral health profile of participants of an elderly cohabitation program in the state of Santa Catarina, Brazil. *Revista de Odontologia Da UNESP*, *48*, 1–9. https://doi.org/10.1590/1807-2577.06119

Lee, E., & Lee, S. W. (2019). Prevalence of periodontitis and its association with reduced pulmonary function: Results from the Korean national health and nutrition examination survey. *Medicina (Lithuania)*, *55*(9), 1–9. https://doi.org/10.3390/medicina55090581

Lee, K., & Kim, J. (2019). Dairy food consumption is inversely associated with the prevalence of periodontal disease in Korean adults. *Nutrients*, *11*(5). https://doi.org/10.3390/nu11051035

Lee, S.-W., Lim, H.-J., & Lee, E. (2017). Association Between Asthma and Periodontitis: Results From the Korean National Health and Nutrition Examination Survey. *Journal of Periodontology*, *88*(6), 575–581. https://doi.org/10.1902/jop.2017.160706

Machado, V., Botelho, J., Mascarenhas, P., Cavacas, M. A., Alves, R., & Mendes, J. J. (2018). Partial recording protocols performance on the assessment of periodontitis severity and extent: Bias magnitudes, sensibility, and specificity. *Revista Portuguesa de Estomatologia, Medicina Dentaria e Cirurgia Maxilofacial*, *59*(3), 145–153. https://doi.org/10.24873/j.rpemd.2018.11.239

Machado, V., Botelho, J., Proença, L., & Mendes, J. J. (2020). Self-reported illness perception and oral health-related quality of life predict adherence to initial

periodontal treatment. *Journal of Clinical Periodontology*, *47*(10), 1209–1218. https://doi.org/10.1111/jcpe.13337

Machado, V., Botelho, J., Viana, J., Pereira, P., Lopes, L. B., Proença, L., Delgado, A. S., & Mendes, J. J. (2021). Association between Dietary Inflammatory Index and Periodontitis: A Cross-Sectional and Mediation Analysis. *Nutrients*, *13*(4), 1194.

Machado, V., Escalda, C., Proença, L., Mendes, J. J., & Botelho, J. (2020). Is there a bidirectional association between polycystic ovarian syndrome and periodontitis? A systematic review and meta-analysis. *Journal of Clinical Medicine*, *9*(6), 1–16. https://doi.org/10.3390/jcm9061961

Marcenes, W., Kassebaum, N. J., Bernabé, E., Flaxman, A., Naghavi, M., Lopez, A., & Murray, C. J. L. (2013). Global burden of oral conditions in 1990-2010: A systematic analysis. *Journal of Dental Research*, *92*(7), 592–597. https://doi.org/10.1177/0022034513490168

Marouf, N., Cai, W., Said, K. N., Daas, H., Diab, H., Chinta, V. R., Hssain, A. A., Nicolau, B., Sanz, M., & Tamimi, F. (2021). Association between periodontitis and severity of COVID-19 infection: A case–control study. *Journal of Clinical Periodontology*, *48*(4), 483–491. https://doi.org/10.1111/jcpe.13435

Marsh, P. D. (2004). Dental plaque as a microbial biofilm. *Caries Research*, *38*(3), 204–211. https://doi.org/10.1159/000077756

McGuinness, L. A., & Higgins, J. P. T. (2021). Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. *Research Synthesis Methods*, *12*(1), 55–61. https://doi.org/10.1002/jrsm.1411

Meyle, J., & Chapple, I. (2015). Molecular aspects of the pathogenesis of periodontitis. *Periodontology 2000*, *69*(1), 7–17. https://doi.org/10.1111/prd.12104

Montero, E., Herrera, D., Sanz, M., Dhir, S., Dyke, T. Van, & Sima, C. (2019). Development and validation of a predictive model for periodontitis using NHANES 2011–2012 data. *Journal of Clinical Periodontology*, *46*(4), 420–429. https://doi.org/10.1111/jcpe.13098.Development

Moya, P. R., Chappuzeau, E., Caro, J. C., & Monsalves, M. J. (2014). Situación de salud oral y calidad de vida de los adultos mayores. *Revista Estomatológica Herediana*, *22*(4), 197. https://doi.org/10.20453/reh.v22i4.85

Muñoz Aguilera, E., Suvan, J., Buti, J., Czesnikiewicz-Guzik, M., Barbosa Ribeiro, A., Orlandi, M., Guzik, T. J., Hingorani, A. D., Nart, J., & D'Aiuto, F. (2020). Periodontitis is associated with hypertension: A systematic review and meta-

analysis. *Cardiovascular Research*, *116*(1), 28–39. https://doi.org/10.1093/cvr/cvz201

Murray, C. J. L., Ezzati, M., Flaxman, A. D., Lim, S., Lozano, R., Michaud, C., Naghavi, M., Salomon, J. A., Shibuya, K., Vos, T., Wikler, D., & Lopez, A. D. (2012). GBD 2010: Design, definitions, and metrics. *The Lancet*, *380*(9859), 2063–2066. https://doi.org/10.1016/S0140-6736(12)61899-6

Nakamura, M., Shigeishi, H., Cheng-Yih, S. U., Sugiyama, M., & Ohta, K. (2020). Oral human cytomegalovirus prevalence and its relationships with periodontitis and Porphyromonas gingivalis in Japanese adults: a cross-sectional study. *Journal of Applied Oral Science : Revista FOB*, *28*, e20200501. https://doi.org/10.1590/1678-7757-2020-00501

Nibali, L. (2018). Development of the gingival sulcus at the time of tooth eruption and the influence of genetic factors. *Periodontology 2000*, *76*(1), 53–42. https://doi.org/10.1111/prd.12158

Oliveira, L. M., Cerezer, D. M., Casarin, M., Moreira, C. H. C., & Zanatta, F. B. (2021). Alcohol use disorders are associated with higher prevalence of periodontitis in a rural area of Brazil. *Journal of Periodontal Research*, *56*(5), 940–950. https://doi.org/10.1111/jre.12890

Ortiz, A. P., González, D., Ramos, J., Muñoz, C., Reyes, J. C., & Pérez, C. (2018). Association of marijuana use with oral HPV infection and periodontitis among Hispanic adults: Implications for oral cancer prevention. *Journal of Periodontology*, *89*(5), 540–548. https://doi.org/10.1002/JPER.17-0372.Association

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., … Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *The BMJ*, *372*. https://doi.org/10.1136/bmj.n71

Page, R. C., & Eke, P. I. (2007). Case Definitions for Use in Population-Based Surveillance of Periodontitis. *Journal of Periodontology*, *78*(7s), 1387–1399. https://doi.org/10.1902/jop.2007.060264

Papapanou, P. N., Park, H., Cheng, B., Kokaras, A., Paster, B., Burkett, S., Watson, C. W., Annavajhala, M. K., Uhlemann, A.-C., & Noble, J. M. (2020). *Subgingival*

microbiome and clinical periodontal status in an elderly cohort: The WHICAP ancillary study of oral health. *91*(Suppl 1), S56–S67. https://doi.org/10.1002/JPER.20-0194.Subgingival

Peres, M. A., Macpherson, L. M. D., Weyant, R. J., Daly, B., Venturelli, R., Mathur, M. R., Listl, S., Celeste, R. K., Guarnizo-Herreño, C. C., Kearns, C., Benzian, H., Allison, P., & Watt, R. G. (2019). Oral diseases: a global public health challenge. *The Lancet*, *394*(10194), 249–260. https://doi.org/10.1016/S0140-6736(19)31146-8

Petersen, P. E., & Ogawa, H. (2012). The global burden of periodontal disease: Towards integration with chronic disease prevention and control. *Periodontology 2000*, *60*(1), 15–39. https://doi.org/10.1111/j.1600-0757.2011.00425.x

Pinto-Filho, J. M., Ribeiro, L. S. F., Sartori, L., dos Santos, J. N., Ramalho, L. M. P., & Cury, P. R. (2018). Association between alcohol dependence and both periodontal disease and tooth loss: a cross-sectional study. *Environmental Science and Pollution Research*, *25*(29), 29089–29095. https://doi.org/10.1007/s11356-018-2807-3

Preshaw, P. M., Alba, A. L., Herrera, D., Jepsen, S., Konstantinidis, A., Makrilakis, K., & Taylor, R. (2012). Periodontitis and diabetes: A two-way relationship. *Diabetologia*, *55*(1), 21–31. https://doi.org/10.1007/s00125-011-2342-y

Ra, Y. J., Tak, Y. J., Kim, Y. J., Lee, S. Y., Lee, J. G., Yi, Y. H., Cho, Y. H., Hwang, H. R., Lee, S. H., Park, E. J., & Lee, Y. I. (2020). Association of work patterns and periodontitis prevalence in Korean adults aged 50 years or older: A nationwide representative study. *International Journal of Environmental Research and Public Health*, *17*(11). https://doi.org/10.3390/ijerph17114006

Ramírez, M., Lopera, N. S., López, A. P., Agudelo-suárez, A. A., & Botero, J. E. (2017). *Periodontal disease and its relationship with clinical and sociodemographic variables in adult patients treated in a service/teaching institution*. *21*(3), 160–167.

Reynolds, I., & Duane, B. (2018). Periodontal disease has an impact on patients' quality of life. *Evidence-Based Dentistry*, *19*(1), 14–15. https://doi.org/10.1038/sj.ebd.6401287

Romero-Castro, N. S., Castro-Alarcón, N., Reyes-Fernández, S., Flores-Alfaro, E., Serna-Radilla, V. O., & Parra-Rojas, I. (2020). Periodontal Disease Distribution, Risk Factors, and Importance of Primary Healthcare in the Clinical Parameters

Improvement. *International Journal of Odontostomatology*, *14*(2), 183–190. https://doi.org/10.4067/s0718-381x2020000200183

Sakurai, A., Yamada, S. I., Karasawa, I., Kondo, E., & Kurita, H. (2021). Accuracy of a salivary examination kit for the screening of periodontal disease in a group medical check-up (Japanese-specific health check-up). *Medicine*, *100*(6), e24539. https://doi.org/10.1097/MD.0000000000024539

Schmidt, J. C., Vogt, S., Imboden, M., Schaffner, E., Grize, L., Zemp, E., Probst-Hensch, N., & Zitzmann, N. U. (2020). Dental and periodontal health in a Swiss population-based sample of older adults: a cross-sectional study. *European Journal of Oral Sciences*, *128*(6), 508–517. https://doi.org/10.1111/eos.12738

Schünemann, H. J., Oxman, A. D., Brozek, J., Glasziou, P., Jaeschke, R., Vist, G. E., Williams, J. W., Kunz, R., Craig, J., Montori, V. M., Bossuyt, P., Guyatt, G. H., & Group, G. W. (2008). Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. *BMJ*, *336*(7653), 1106–1110. https://doi.org/10.1373/clinchem.2008.117614

Schwarzer, G. (2007). *meta: An R Package for Meta- Analysis* (7th ed.). R News.

Schwarzer, G., Carpenter, J. R., & Rücker, G. (2015). *Meta-Analysis with R (1st ed.)* (1st ed.). Springer.

Sekiguchi, A., Kawashiri, S. ya, Hayashida, H., Nagaura, Y., Nobusue, K., Nonaka, F., Yamanashi, H., Kitamura, M., Kawasaki, K., Fukuda, H., Iwasaki, T., Saito, T., & Maeda, T. (2020). Association between high psychological distress and poor oral health-related quality of life (OHQoL) in Japanese community-dwelling people: the Nagasaki Islands Study. *Environmental Health and Preventive Medicine*, *25*(1), 1–9. https://doi.org/10.1186/s12199-020-00919-9

Shamsoddin, E. (2021). Is periodontitis associated with the severity of COVID-19? *Evidence-Based Dentistry*, *22*(2), 66–68. https://doi.org/10.1038/s41432-021-0179-x

Shariff, J. A., Ahluwalia, K. P., & Papapanou, P. N. (2017). Relationship Between Frequent Recreational Cannabis (Marijuana and Hashish) Use and Periodontitis in Adults in the United States: National Health and Nutrition Examination Survey 2011 to 2012. *Journal of Periodontology*, *88*(3), 273–280. https://doi.org/10.1902/jop.2016.160370

Shariff, J. A., Burkett, S., Watson, C. W., Cheng, B., Noble, J. M., & Papapanou, P. N. (2018). Periodontal Status among Elderly Inhabitants of Northern Manhattan.

Journal of Clinical Periodontology, *145*(8), 909–919. https://doi.org/10.1111/jcpe.12927.Periodontal

Shimizu, Y., Yamanashi, H., Kitamura, M., Furugen, R., Iwasaki, T., Fukuda, H., Hayashida, H., Kawasaki, K., Kiyoura, K., Kawashiri, S. Y., Saito, T., Kawakami, A., & Maeda, T. (2019). Association between human T cell leukemia virus type-1 (HTLV-1) infection and advanced periodontitis in relation to atherosclerosis among elderly Japanese: A cross-sectional study. *Environmental Health and Preventive Medicine*, *24*(1), 1–9. https://doi.org/10.1186/s12199-019-0836-2

Shyagali, T. R., Salama, M. H., & Bhayya, D. P. (2017). Prevalence of tobacco usage and its effect on the periodontal health parameters in the mining employees and the general population - A comparative study. *Brazilian Journal of Oral Sciences*, *16*, 1–9. https://doi.org/10.20396/bjos.v16i0.8650489

Silva-Junior, M. F., Batista, M. J., & da Luz Rosário de Sousa, M. (2019). Risk factors for tooth loss in adults: A population-based prospective cohort study. *PLoS ONE*, *14*(7), 1–14. https://doi.org/10.1371/journal.pone.0219240

Silva-Junior, M. F., de Sousa, A. C. C., Batista, M. J., & de Sousa, M. da L. R. (2017). Oral health condition and reasons for tooth extraction among an adult population (20-64 years old). *Ciencia e Saude Coletiva*, *22*(8), 2693–2702. https://doi.org/10.1590/1413-81232017228.22212015

Sim, H. Y., Kim, H. S., Jung, D. U., Lee, H., Lee, J. W., Han, K., & Yun, K. I. (2017). Association between orthodontic treatment and periodontal diseases: Results from a national survey. *Angle Orthodontist*, *87*(5), 651–657. https://doi.org/10.2319/030317-162.1

Singh, A., Shrestha, A., Bhagat, T. K., & Baral, D. D. (2020). Assessment of oral health status and treatment needs among people of Foklyan area, Dharan, Nepal. *BMC Oral Health*, *20*(1), 1–9. https://doi.org/10.1186/s12903-020-01312-2

Skoskiewicz-Malinowska, K., Malicka, B., Zietek, M., & Kaczmarek, U. (2018). Oral health condition and occurrence of depression in the elderly. *Medicine*, *97*, 41.

Song, E., Park, M. J., Kim, J. A., Roh, E., Yu, J. H., Kim, N. H., Yoo, H. J., Seo, J. A., Kim, S. G., Kim, N. H., Baik, S. H., & Choi, K. M. (2021). Implication of thyroid function in periodontitis: a nationwide population-based study. *Scientific Reports*, *11*(1), 1–8. https://doi.org/10.1038/s41598-021-01682-9

Song, Y. H., Ahn, Y. B., Shin, M. S., Brennan, D., & Kim, H. D. (2021). Association of periodontitis with oral malodor in Korean adults. *PLoS ONE*, *16*(3 March), 1–15.

https://doi.org/10.1371/journal.pone.0247947

Stødle, I. H., Verket, A., Høvik, H., Sen, A., & Koldsland, O. C. (2021). Prevalence of periodontitis based on the 2017 classification in a Norwegian population: The HUNT study. *Journal of Clinical Periodontology*, *48*(9), 1189–1199. https://doi.org/10.1111/jcpe.13507

Su, C.-Y., Shigeishi, H., Murodumi, H., Sugiyama, M., Ohta, K., & Takemoto, T. (2021). Association of oral Epstein-Barr virus with periodontal health in Japanese adults. *Experimental and Therapeutic Medicine*, *22*(1), 1–8. https://doi.org/10.3892/etm.2021.10199

Sun, H., Du, M., Tai, B., Chang, S., Wang, Y., & Jiang, H. (2020). Prevalence and associated factors of periodontal conditions among 55- to 74-year-old adults in China: results from the 4th National Oral Health Survey. *Clinical Oral Investigations*, *24*(12), 4403–4412. https://doi.org/10.1007/s00784-020-03306-4

Suominen, A. L., Varsio, S., Helminen, S., Nordblad, A., Lahti, S., & Knuuttila, M. (2018). Dental and periodontal health in Finnish adults in 2000 and 2011. *Acta Odontologica Scandinavica*, *76*(5), 305–313. https://doi.org/10.1080/00016357.2018.1451653

Thanakun, S., Watanabe, H., Thaweboon, S., & Izumi, Y. (2014). Association of Untreated Metabolic Syndrome With Moderate to Severe Periodontitis in Thai Population. *Journal of Periodontology*, *85*(11), 1502–1514. https://doi.org/10.1902/jop.2014.140105

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 Periodontology*, *89*(February), S159–S172. https://doi.org/10.1002/JPER.18-0006

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. https://doi.org/10.1111/ijlh.12426

Tran, D. T., Gay, I., Du, X. L., Fu, Y., Bebermeyer, R. D., Neumann, A. S., Streckfus, C., Chan, W., & Walji, M. F. (2013). Assessing periodontitis in populations: A systematic review of the validity of partial-mouth examination protocols. *Journal of Clinical Periodontology*, *40*(12), 1064–1071. https://doi.org/10.1111/jcpe.12165

Tran, D. T., Gay, I., Du, X. L., Fu, Y., Bebermeyer, R. D., Neumann, A. S., Streckfus,

C., Chan, W., & Walji, M. F. (2014). Assessment of partial-mouth periodontal examination protocols for periodontitis surveillance. *Journal of Clinical Periodontology*, *41*(9), 846–852. https://doi.org/10.1111/jcpe.12285

Vallespir, C. A., Ulloa Ortega, C., Luengo Machuca, L., Rodriguez Vera, M., & Contreras Silva, S. (2014). Grado de concordancia de los índices más utilizados en estudios epidemiológicos de la enfermedad periodontal. *Revista Clínica de Periodoncia, Implantología y Rehabilitación Oral*, *7*(3), 175–179. https://doi.org/10.1016/j.piro.2014.07.003

Vano, M., Gennai, S., Karapetsa, D., Miceli, M., Giuca, M. R., Gabriele, M., & Graziani, F. (2015). The influence of educational level and oral hygiene behaviours on DMFT index and CPITN index in an adult Italian population: An epidemiological study. *International Journal of Dental Hygiene*, *13*(2), 151–157. https://doi.org/10.1111/idh.12098

Wahlin, Å., Papias, A., Jansson, H., & Norderyd, O. (2018). Secular trends over 40 years of periodontal health and disease in individuals aged 20–80 years in Jönköping, Sweden: Repeated cross-sectional studies. *Journal of Clinical Periodontology*, *45*(9), 1016–1024. https://doi.org/10.1111/jcpe.12978

Wang, J., Lv, J., Wang, W., & Jiang, X. (2016). Alcohol consumption and risk of periodontitis: A meta-analysis. *Journal of Clinical Periodontology*, *43*(7), 572–583. https://doi.org/10.1111/jcpe.12556

Watt, R. G., Daly, B., Allison, P., Macpherson, L. M. D., Venturelli, R., Listl, S., Weyant, R. J., Mathur, M. R., Guarnizo-Herreño, C. C., Celeste, R. K., Peres, M. A., Kearns, C., & Benzian, H. (2019). Ending the neglect of global oral health: time for radical action. *The Lancet*, *394*(10194), 261–272. https://doi.org/10.1016/S0140-6736(19)31133-X

Whitmore, S. E., & Lamont, R. J. (2014). Oral Bacteria and Cancer. *PLoS Pathogens*, *10*(3), 1–3. https://doi.org/10.1371/journal.ppat.1003933

Wu, L., Zhang, S. Q., Zhao, L., Ren, Z. H., & Hu, C. Y. (2022). Global, regional, and national burden of periodontitis from 1990 to 2019: Results from the Global Burden of Disease study 2019. *Journal of Periodontology*. https://doi.org/10.1002/JPER.21-0469

Zaitsu, T., Kanazawa, T., Shizuma, Y., Oshiro, A., Takehara, S., Ueno, M., & Kawaguchi, Y. (2017). Relationships between occupational and behavioral parameters and oral health status. *Industrial Health*, *55*(4), 381–390.

https://doi.org/10.2486/indhealth.2017-0011

Zhao, M. J., Qiao, Y. X., Wu, L., Huang, Q., Li, B. H., & Zeng, X. T. (2019). Periodontal disease is associated with increased risk of hypertension: A cross-sectional study. *Frontiers in Physiology*, *10*(APR), 1–8. https://doi.org/10.3389/fphys.2019.00440

VIII. APPENDICES

Supplementary file 1 – **PRISMA Checklist** (M. J. Page et al., 2021)

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	13-21
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	22
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	23
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	24
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	24
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	24
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	25
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	25
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	25

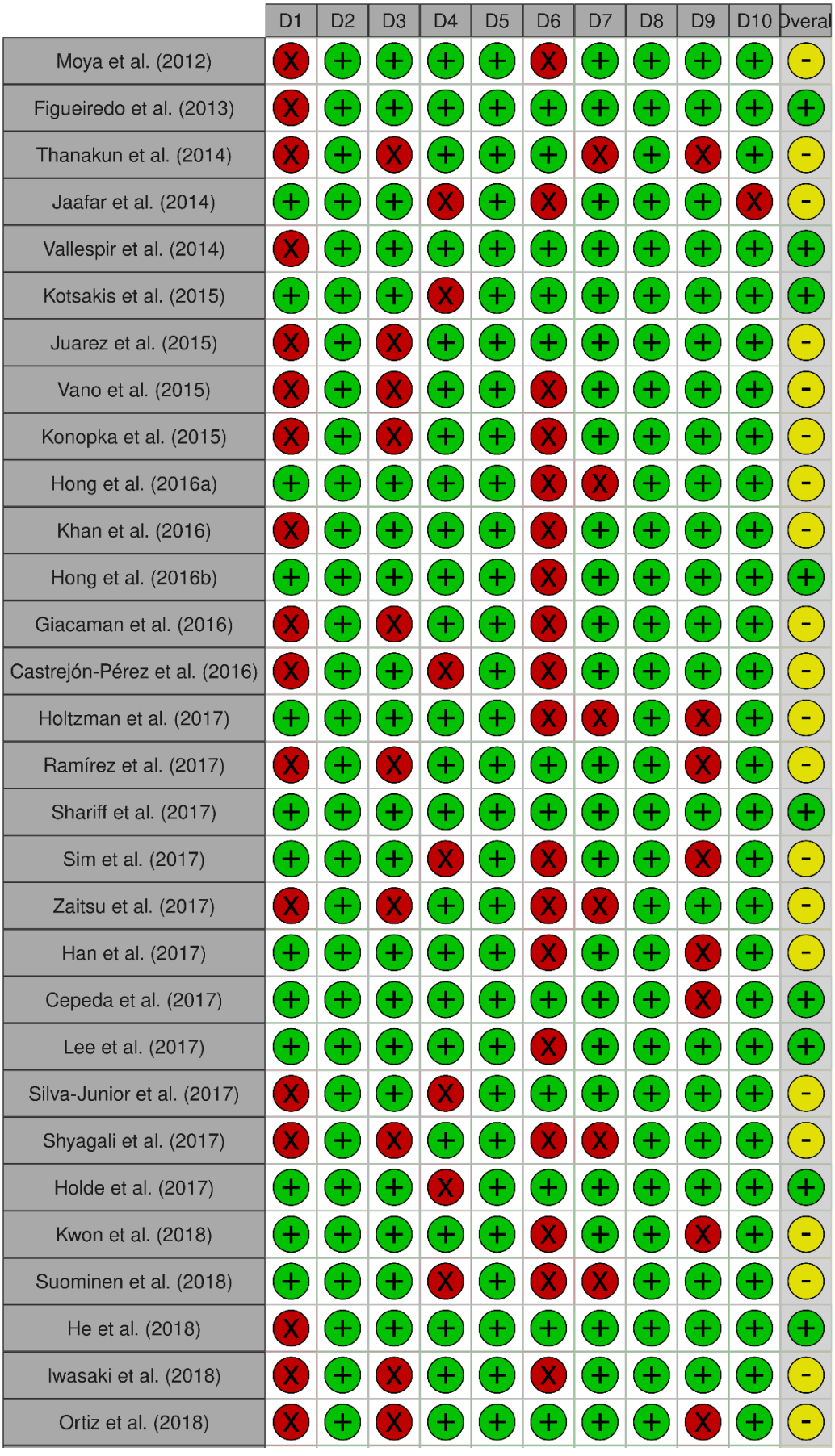
Section and Topic	Item #	Checklist item	Location where item is reported
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	26
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	27
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	29
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	29
Study characteristics	17	Cite each included study and present its characteristics.	30-44
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	45-46
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	45-46

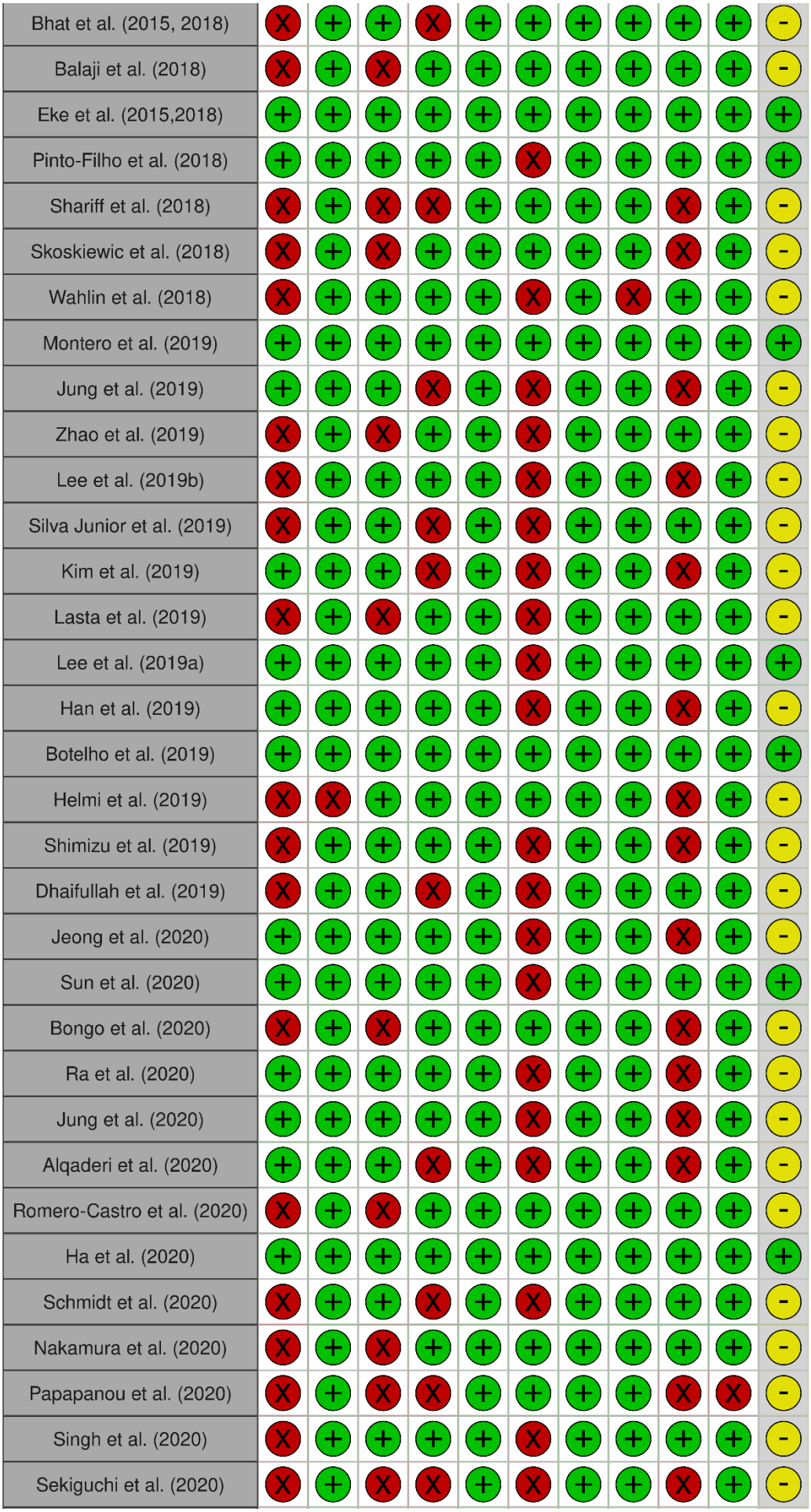
Section and Topic	Item #	Checklist item	Location where item is reported
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	51
	23b	Discuss any limitations of the evidence included in the review.	51-52
	23c	Discuss any limitations of the review processes used.	51-52
	23d	Discuss implications of the results for practice, policy, and future research.	52
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	23
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	
Competing interests	26	Declare any competing interests of review authors.	
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

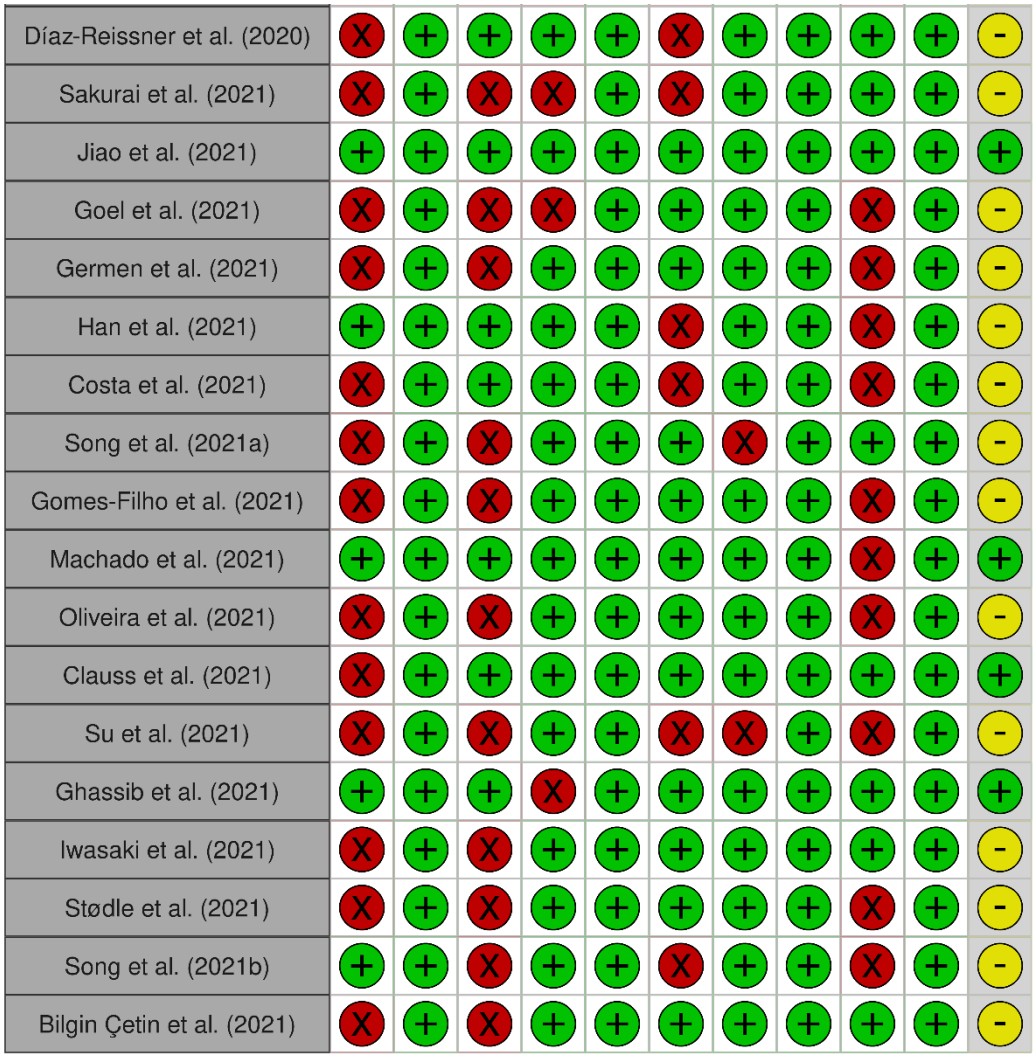
Supplementary file 2 – **Prisma Abstract Checklist** (M. J. Page et al., 2021)

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	No
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	No
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	No
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	No
Registration	12	Provide the register name and registration number.	No

Supplementary file 3 – **Summary Plot of the Methodological quality of included studies** (McGuinness & Higgins, 2021)




Bhat et al. (2015, 2018)
Balaji et al. (2018)
Eke et al. (2015,2018)
Pinto-Filho et al. (2018)
Shariff et al. (2018)
Skoskiewic et al. (2018)
Wahlin et al. (2018)
Montero et al. (2019)
Jung et al. (2019)
Zhao et al. (2019)
Lee et al. (2019b)
Silva Junior et al. (2019)
Kim et al. (2019)
Lasta et al. (2019)
Lee et al. (2019a)
Han et al. (2019)
Botelho et al. (2019)
Helmi et al. (2019)
Shimizu et al. (2019)
Dhaifullah et al. (2019)
Jeong et al. (2020)
Sun et al. (2020)
Bongo et al. (2020)
Ra et al. (2020)
Jung et al. (2020)
Alqaderi et al. (2020)
Romero-Castro et al. (2020)
Ha et al. (2020)
Schmidt et al. (2020)
Nakamura et al. (2020)
Papapanou et al. (2020)
Singh et al. (2020)
Sekiguchi et al. (2020)


Díaz-Reissner et al. (2020)
Sakurai et al. (2021)
Jiao et al. (2021)
Goel et al. (2021)
Germen et al. (2021)
Han et al. (2021)
Costa et al. (2021)
Song et al. (2021a)
Gomes-Filho et al. (2021)
Machado et al. (2021)
Oliveira et al. (2021)
Clauss et al. (2021)
Su et al. (2021)
Ghassib et al. (2021)
Iwasaki et al. (2021)
Stødle et al. (2021)
Song et al. (2021b)
Bilgin Çetin et al. (2021)
D1: Was the study's target population a close representation of the national population in relation to relevant variables?
D2: Was the sampling frame a true or close representation of the target population?
D3: Was some form of random selection used to select the sample, OR was a census undertaken?
D4: Was the likelihood of nonresponse bias minimal?
D5: Were data collected directly from the subjects (as opposed to a proxy)?
D6: Was an acceptable case definition used in the study?
D7: Was the study instrument that measured the parameter of interest shown to have validity and reliability?
D8: Was the same mode of data collection used for all subjects?
D9: Was the length of the shortest prevalence period for the parameter of interest appropriate?
D10: Were the numerator(s) and denominator(s) for the parameter of interest appropriate?
High Risk of Bias
Moderate Risk of Bias
Low Risk of Bias