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SYSTEMATIC REVIEW

Effect of orthodontic therapy in periodontitis and non-periodontitis patients: a systematic review with meta-analysis

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Abstract

Aim: To answer these PICO questions:

#1: In adult patients with malocclusion, what are the effects of orthodontic tooth movement (OTM) on clinical attachment level (CAL) changes in treated periodontitis patients with a healthy but reduced periodontium compared to non-periodontitis patients?

#2: In adult patients with treated periodontitis and malocclusion, which is the efficacy of skeletal anchorage devices compared to conventional systems in terms of orthodontic treatment outcomes?

Material and methods: Seven databases were searched until June 2020 looking for randomized, non-randomized trials and case series. Mean effects (ME) and 95% confidence intervals (CIs) were calculated.

Results: Twenty-six studies with high risk of bias were included.

PICO#1: In 26 patients without periodontitis and in 69 treated periodontitis patients, minimal changes in periodontal outcomes were reported after orthodontic therapy ($p > 0.05$). A significant CAL gain (mm) (ME = 3.523; 95% CI [2.353; 4.693]; $p < 0.001$) was observed in 214 patients when periodontal outcomes were retrieved before a combined periodontal and orthodontic therapy.

PICO#2: Orthodontic variables were scarcely reported, and objective assessment of the results on orthodontic therapy was missing.

Conclusions: Based on a small number of low-quality studies, in non-periodontitis and in stable treated periodontitis patients, OTM had no significant impact on periodontal outcomes.

KEYWORDS
anchorage, clinical attachment level, non-periodontitis, orthodontic treatment, periodontitis

1 | INTRODUCTION

Stage IV periodontitis is characterized by periodontal interdental attachment loss, formation of pockets, bony defects and possible pathologic tooth migration. This periodontal condition requires complex multidisciplinary rehabilitation due to masticatory dysfunction, secondary occlusal trauma, bite collapse and drifting and flaring of the remaining teeth and risk for loss of dentition (Papapanou et al., 2018; Tonetti & Sanz, 2019). Orthodontic therapy can help realigning

the migrated teeth and distributing the edentulous spaces. If the periodontal inflammation remains uncontrolled during the orthodontic treatment, this will accelerate the progression of periodontal destruction leading to further loss of attachment (Wennström et al., 1993). A recent systematic review concluded that orthodontic treatment with fixed appliances has little to no clinically relevant effect on clinical attachment levels (CAL) on healthy adults or adolescents (Papageorgiou et al., 2018). Although these treatment-induced changes are mostly transient and normalize after removal of orthodontic appliances in long-term follow-ups (Gomes et al., 2007), some authors reported that clinical and microbial periodontal parameters were only partly normalized 3 months following the removal of the appliances (van Gastel et al., 2011). Moreover, and according to another systematic review, orthodontic fixed retainers seem to be a retention strategy rather compatible with periodontal health, or at least not related to severe detrimental effects on the periodontium. (Arn et al., 2020) To our knowledge, there are not systematic reviews evaluating the effect of orthodontic tooth movement (OTM) on CAL levels in periodontitis patients.

Another aspect that cannot be overlooked is the effect of OTM in patients with a reduced periodontium, where the total surface of the periodontal ligament that receives the orthodontic forces is significantly less and the tooth centre of resistance is apically displaced, resulting in the expression of greater moments of force. In these situations, the orthodontic treatment requires significant experience on the end of the orthodontist and should be carefully planned and monitored in order to achieve bodily instead of tipping tooth movements (Melsen et al., 1989). The presence of reduced periodontal support also implies different anchorage requirements. Control of anchorage during orthodontic treatment is considered of significant importance since it helps to avoid undesirable tooth movements that take place as a consequence of the reaction forces applied to move teeth (Gkantidis et al., 2010). In many occasions, the use of skeletal anchorage devices, such as temporary anchorage devices (TADs), orthodontic microscrews or mini-plates, or conventional dental implants are recommended for a better control of three-dimensional tooth movements (Kanomi, 1997; Liu et al., 2016; Ödman et al., 1994; Sugawara et al., 2004). Moreover, the growing demand for minimal patient compliance during OTM (Nanda & Kierl, 1992) and the need to use the simplest orthodontic system for reducing plaque accumulation as much as possible (Gkantidis et al., 2010) has made the use of TADs more promising as an excellent alternative to traditional orthodontic anchorage. However, although they are widely recognized as valuable tools to facilitate tooth movements, there is little evidence showing their advantages compared to conventional anchorage systems in patients with periodontitis.

Therefore, the aim of this systematic review was to answer the following PICO questions:

- PICO #1: In adult patients with malocclusion (population), what are the effects of OTM on clinical attachment level (CAL) changes (outcome) in treated periodontitis patients with a healthy but reduced periodontium (exposure) compared to non-periodontitis patients (comparator)?
- PICO #2: In adult patients with malocclusion and healthy but reduced periodontium (population), what is the efficacy of skeletal anchorage devices (implants or TADs – microscrews or miniplates–) (intervention) compared to conventional anchorage systems (comparator), in terms of orthodontic treatment (outcomes)?

CLINICAL RELEVANCE

Scientific rationale for the study: Stage IV periodontitis patients usually need orthodontic therapy due to pathologic tooth migration. More information about its effects is needed.

Principal findings: In non-periodontitis and in stable treated periodontitis patients, orthodontic therapy led to minimal changes in periodontal outcomes. In untreated periodontitis patients, significant improvements in periodontal outcomes were observed after periodontal and orthodontic therapies were successfully completed. Assessment of the orthodontic outcomes was poorly reported, and no quantitative comparisons were possible.

Practical implications: Patients with reduced periodontium but stable periodontal status seem to receive orthodontic tooth movement with minimal or no additional loss of attachment.

2 | MATERIAL AND METHODS

2.1 | Protocol development and systematic review reporting

Two protocols were prepared according to the guidelines set by PROSPERO (National Institute of Health Research, UK). The conduct and reporting of the review followed guidelines from the Cochrane handbook (Cumpston et al., 2019) and the PRISMA (Preferred Reporting Items for Systematic Review and Meta-analysis) statement (Liberati et al., 2009; Moher et al., 2009; Page et al., 2020) and its extension for abstracts (Beller et al., 2013).

The protocols were presented to the Workshop Committee for the XVII European Workshop on Periodontology. Before starting the study, the protocols were approved and registered in the International Prospective Register of Systematic Reviews PROSPERO (CRD42020177549 and CRD42020178550).

2.2 | Eligibility criteria

Table 1 shows the main inclusion criteria for both PICOS questions, including primary and secondary outcomes.

TABLE 1 Components of both PICOS questions

	PICO #1	PICO #2	Common components for both PICOS
P Patients	Adult patients with malocclusion treated with orthodontic fixed appliance (possible subgroup analysis considering other orthodontic appliances).	Periodontally stable, previously treated periodontitis adult patients undergoing orthodontic treatment.	Individuals of ethnicity, sex, older than 18 years.
I Intervention or exposure	Treated periodontitis patients with a healthy but reduced periodontium (Papapanou et al., 2018; Tonetti & Sanz, 2019) (possible specific analysis on stage IV periodontitis patients).	Anchorage provided with TADs or implants ('skeletal' anchorage).	
C Comparison	Non-periodontitis patients.	Anchorage provided with conventional methods (no TADs, no implants).	
O Outcomes	*Primary outcome*: changes in mean CAL (mm) before orthodontic treatment and after appliance removal, or follow-up period of at least 6 months. Comparisons considered: differences throughout orthodontic treatment or differences between treated periodontitis patients versus non-periodontitis patients. *Secondary outcomes*: root resorption, inflammatory cytokines levels, timing of force application after periodontal therapy, tooth loss, tooth mobility, gingival profile (gingival recessions and papilla index), duration of OTM, success of OTM, subjective and objective measures of masticatory function.	Primary outcome: orthodontic treatment outcome, evaluated using different indices (occlusal, treatment need, quality of orthodontic finishing) (Brook & Shaw, 1989; Cangialosi et al., 2004; Casko et al., 1998; Richmond et al., 1992) and/or occlusal features (Angle's classification of molars, overjet, and overbite) on post-treatment dental casts and/or cephalometric changes (analysing pre-treatment and post-treatment). *Secondary outcomes*: Implant or TAD failure rate, mesiodistal 'loss of anchorage', 'anchorage loss ratio' (Papadopoulos et al., 2011). Clinical attachment levels changes (mm).	**Secondary outcomes:** changes in probing pocket depth (mm), recession (mm), bleeding on probing (%), gingival index, plaque level (PII), alveolar bone level and orthodontic treatment duration. Secondary patient-based outcomes: patient-reported outcome measures (PROMs), possible adverse effects and oral health-related quality of life, patient satisfaction, discomfort, hygiene difficulty, etc. Any study reporting at least one of the primary/secondary outcomes were considered for inclusion.
S Study design and duration			RCTs, CCTs, prospective or retrospective clinical cohort studies or case series studies with pre- and post-treatment measures with at least 6 months of follow-up were included.

Abbreviations: CAL, clinical attachment level; CCTs, controlled clinical trials; OTM, orthodontic tooth movement; RCTs, randomized clinical trials; TAD, temporary anchorage devices.

Studies were excluded if: (1) they were done specifically on patients with diabetes or any known systemic condition or any drugs intake that might influence orthodontic treatment (bone remodelling); (2) they were preclinical *in vivo* studies (experimental animal studies), non-clinical studies and studies with experimentally induced periodontal disease; (3) pertained to skeletal and not dental movement (e.g. maxillary expansion); (4) studies with ectopic/displaced canines, combined orthodontic-orthognathic surgical cases and other surgically assisted techniques. Due to time limitations, only papers published in English were selected.

2.3 | Information sources and search

Two systematic searches were conducted for published, unpublished and ongoing studies up to June 2020 by two investigators (CM, EF). The search strategy and the seven databases searched are presented in Appendix S1 and Appendix S2. Reference lists of retrieved papers and previously published systematic reviews were also hand searched. Grey literature was not excluded from our search.

2.4 | Study selection

Study selection was based on a two-step approach: (1) Screening of titles and abstracts and (2) full-text analysis. Two reviewers per PICO question (NA and JB and BC and GA) selected eligible studies by reviewing the titles and abstracts and considering the inclusion and exclusion criteria. The complete articles sourced via eligible titles and abstracts were obtained and examined independently to determine eligibility. Discrepancies pertaining to the inclusion of any specific paper were discussed until either a consensus was reached or a third reviewer determined inclusion or exclusion (CM, EF). All reports excluded at this stage and reasons for their exclusion were registered.

Inter-observer agreement value for the screening of complete articles was assessed via kappa score.

2.5 | Risk of bias in individual studies

Risk of bias assessments was conducted for methodological quality of each included study using the critical appraisal tool most appropriate for its design.

- For randomized controlled trials (RCTs) or controlled clinical trials (CCTs), the quality assessment was undertaken following the Cochrane RoB 2.0 tool (Sterne et al., 2019) and the ROBINS-I (Risk Of Bias In Non-randomized Studies - of Interventions) tool (Sterne et al., 2016), respectively.
- The Newcastle–Ottawa scale (NOS) was used for cohort studies (Wells et al., 2015).
- The National Institute of Health's quality assessment tool was used for uncontrolled studies with two consecutive measurements (NHLBI, 2014).

All risk of bias assessments were performed at the study level using CAL as outcome. If the previous was not available, a secondary outcome was used.

2.6 | Data collection process

Based on the Cochrane recommendations, standardized, pre-piloted data extraction forms were designed. Characteristics of included trials and numerical data were extracted. A thorough calibration of the data extraction process took place using predefined data extraction forms amongst four reviewers (NA, JB, GA and BC). Data were extracted by these reviewers (NA, JB, GA and BC), who achieved consensus on which data to extract from the included studies, under the supervision of two reviewers (EF, CM).

All outcome variables for which data were sought (primary and secondary outcomes) for both PICOS questions are listed in Table 1. Data on reported outcomes were extracted at baseline (before orthodontic therapy) and immediately after orthodontic therapy (either the exact value in each visit or the change between visits) or after at least 6 months from baseline. In case authors provided data on longer follow-up periods, these data were not registered. In case of missing data, authors were contacted and their responses were registered.

Studies without sufficient data to enter the meta-analyses were kept in the systematic review and analysed qualitatively.

2.7 | Data analyses

To summarize and compare studies, mean changes between final and baseline visits and standard errors (SE) values were directly pooled and analysed with mean effects (ME) and 95% confidence intervals (CIs). When the differences between (Δ) baseline-end were not reported, they were calculated using the formula: ΔVar = Var2 − Var1, where Var1 was the mean value before treatment and Var2 the mean value after treatment. In addition, the variance of ΔVar was estimated with the formula: $SVar^2 = SVar1^2 + SVar2^2 - (2*r*SVar1*SVar2)$, where $SVar^2$ was the variance of the difference, $SVar1^2$ is the variance of the mean baseline value, and $Svar2^2$ is the variance of the mean end value. A correlation r of 0.5 was assumed as described before (Paraskevas et al., 2008).

In order to compare the changes in study outcomes between baseline and final visits, all study designs were included, but considering each arm of RCTs or CCTs as an independent study (Sanz-Sánchez et al.,2015, 2018). Subgroup analyses were performed based on: (1) periodontal diagnoses; (2) time of baseline periodontal outcomes collection (before or after periodontal therapy); (3) interval between periodontal and orthodontic treatment; (4) type of periodontal surgical therapy; (5) type of orthodontic tooth movement; and (6) type of orthodontic anchorage. A random-effects approach together with the Dersimonian and Laird method for between-study variance was chosen a priori for pooling individual study effects.

The statistical absolute and relative between-trial heterogeneity was assessed using the Tau^2 and the I^2 index, respectively; the latter defined as the percentage of variation in the global estimate that was attributable to heterogeneity (I^2 = 25%: low; I^2 = 50%: moderate; I^2 = 75%: high heterogeneity).

In case of heterogeneity, in addition to the summary estimate (MD) and CI, prediction intervals will be reported to allow more informative inferences and illustrate which range of true effects can be expected in future settings, presenting the heterogeneity in the same metric as the original effect size measure (IntHout et al., 2016).

Forest Plots were created to illustrate the effects in the meta-analysis of the global estimation and the different sub-analyses. STATA®14 (StataCorp LP, Lakeway Drive, College Station, Texas, USA) intercooled software was used to perform all analyses. Statistical significance was set at $p \leq 0.05$.

2.8 | Risk of bias across studies. Strength of the evidence

The overall quality of evidence was rated using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach (Guyatt et al., 2011) following a recent guidance on combining randomized with non-randomized studies (Schunemann et al., 2019) and the summary of findings table format by Carrasco-Labra et al. (Carrasco-Labra et al., 2016). To reach an outcome level grading of evidence, the authors considered risk of bias, inconsistency, imprecision, reporting bias, publication bias, large effects, plausible confounding and dose response gradient as per the GRADE methodology.

TABLE 2 Main characteristics of included studies

First author and Year	Country	Setting	Funding	Centre/s	Study design	Study Duration Mean (SD) [range]
Carvalho et al. (2018)	Brazil	University	None	1	CP	[20–22]
Brown (1973)	United States	University	Partly by USA PHS	1	PCS	[6–7]
Eliasson et al. (1982)	Sweden	University	NR	1	RCS	[8–22]
Melsen et al. (1989)	Denmark	Private	NR	1	PCS	[6–18]
Ödman et al., (1994)	Sweden	University	NR	1	PCS	17 [4–33]
Re et al., (2000)	Italy	Private	NR	1	RCS	144
Corrente et al., (2003)	Italy	Private	NR	1	PCS	10 (2.6)
Cardaropoli et al. (2004, Re (2004)	Italy	Private	NR	1	PCS	O: 11.71 (2.98) Fw: 24
Cardaropoli et al., (2006)	Italy	Private	NR	1	PCS	15
Ghezzi (2008)	Italy	Private	NR	1	PCS	NR
Ogihara (2010)	Japan	Private	NR	1	RCT	12
Attia (2012)	Egypt	University	NR	1	CCT split mouth	12
Lee et al., (2013)	Korea	University	None	1	PCS	35.2
Ghezzi (2013)	Italy	University	NR	1	PCS	9 (3.2)
Heravi (2011), Bayani et al. (2015)	Iran	University	None	1	PCS	O: 7.7 [4.3 – 11.5] Fw: 6
Cao et al., (2015)	China	University	NR	1	PCS	19
Ogihara (2015)	Japan	Private	NR	1	RCT	37
Zasčiurinskienė et al. (2018, 2019a, 2019b)	Lithuania	University & Private	None	3	RCT	21.68 (1.23) 25.73 (1.00)
Zhang (2017)	China	University	NR	1	RCT[a]	36
Attia (2019)	Egypt	University	NR	1	RCT split mouth	9
Aimetti (2020)	Italy	Private	None	1	RCS	O: 18.6 (9) [4–36] Fw: 139.2 (19.2) [120–180]

Time pointsn (months)	Study groups	Author´s conclusion
3 (0; 16–18; 20–22)	Periodontitis and Non-Periodontitis	Aggressive periodontitis with reduced periodontium can undergo orthodontic movement without additional attachment loss.
3 (0; 3–4; 6–7)	Periodontitis	Molar intrusion is an appropriate therapy, where indicated, with favourable periodontal results.
3 (0; 8–22)	Periodontitis	If careful pre-orthodontic oral hygiene treatment is given, no increased progression of periodontitis will occur due to orthodontic tooth movement.
2 (0; 6–18)	Periodontitis	Satisfactory periodontal and aesthetic results can be obtained in anterior teeth with PTM after orthodontic treatment.
2 (0; 17)	Periodontitis	Osseointegrated titanium implants remain stable when orthodontically loaded and may thus serve as anchorage units for tooth movements.
6 (0; 24; 48; 72; 120; 144)	Periodontitis	Orthodontic treatment is no longer a contraindication in the therapy of severe adult periodontitis.
2 (0;10)	Periodontitis	After a proper periodontal therapy, is possible to perform orthodontic intrusion towards intrabony defects in patients with severe periodontal disease; obtaining significant PPD reduction, CAL gain and radiographic bone fill.
3 (0; 11.71; 24)	Periodontitis	Periodontal teeth can be successfully aligned with an adequate orthodontic–periodontic treatment without worsening the clinical and aesthetic outcomes.
2 (0; 10–15)	Periodontitis	Combined periodontic–orthodontic approach for the treatment of intrabony defects, results in the reductions in PPD, gain of CAL and radiographic bone fill.
3 (0; 12; NR)	Periodontitis	Combined orthodontic–periodontal approach that prevents damaging the regenerated periodontal apparatus and produces aesthetic improvements as a result of alignments and enhancement of papilla height.
2 (0; 12)	Periodontitis	EMD/DFDBA and ortho/EMD/DFDBA were effective for the treatment of 2 or 3-wall intrabony defects.
3 (0; 6; 12)	Periodontitis	Combined periodontic–orthodontic therapy resulted in favourable clinical and radiographic results. Greater reductions in PPD and higher CAL gain were obtained in the intrabony defects when immediate orthodontic tooth movement was applied.
3 (0; 5–20; 35.2)	Periodontitis	3D analysis showed the detailed positional changes of overerupted molar which can be successfully intruded.
2 (0; 9)	Periodontitis	Orthodontic movement in immature bone during the healing time, does not adversely affect the maturation process of the entire periodontal apparatus.
3 (0; 4.3–11.5; +6)	Periodontitis	Orthodontic intrusion showed clinical signs of CAL gain and shortening of clinical crown, without affecting negatively the periodontium.
2 (0; 19)	Periodontitis	Orthodontic intrusion improved the periodontal support of migrated incisors.
3 (0; 12; 36)	Periodontitis	Forced eruption with EMD/DFDBA therapies resulted in greater soft and hard tissue improvements compared to forced eruption with EMD alone.
3 (0; 1.38; 21.68) 3 (0; 4.56; 25.73)	Periodontitis Periodontitis	Orthodontic movements in periodontal patients resulted in CAL. gain, PPD reduction, alveolar bone gain and external apical root resorption
3 (0; 6; 18)	Periodontitis	Combined orthodontic-periodontic treatment had good clinical efficacy in the treatment of periodontitis and decreased the levels of inflammatory cytokines. PPD, PI, CAL and sulcus bleeding index measurements were better in the combined orthodontic–periodontic treatment group
3 (0; 6; 9)	Periodontitis	Improvements in clinical and radiographic parameters were observed following the adjunctive low-level laser therapy and orthodontic regenerative therapy for the management of intrabony defects in chronic periodontitis patients
3 (0; 18.6; 139.2)	Periodontitis	Orthodontic tooth movement has no negative effects in patients with a healthy but reduced periodontium, when enrolled in strict maintenance care programme

(Continues)

TABLE 2 (Continued)

First author and Year	Country	Setting	Funding	Centre/s	Study design	Study Duration Mean (SD) [range]
Harris (1990)	United States	University	NR	1	RCS	30 (4.2)
Sadiq (2008)	Iraq	University	NR	1	PCS	16 (4.2)
Karkhanechi et al., (2013)	United States	University	NR	1	CP	12
Rasperini (2017)	Italy	University	Partly by Hu-Friedy Company	1	PCS	9
Zoizner (2018)	Israel	University	NR	1	CR	33.79 (15.97)

Abbreviations: CAL, clinical attachment level; CP, cohort prospective; CR, cohort retrospective; CCT, controlled clinical trial; DFDBA, demineralized freeze-dried bone allograft; DT, during treatment; EMD, enamel matrix derivative; Fw, follow-up; NR, not reported; O, orthodontic treatment; PI, plaque index; PCS, prospective case series; PHS, Public Health Service; PPD, probing pocket depth; PTM, pathologic tooth migration; RCS, retrospective case series; RCT; randomized controlled clinical trial; SD, standard deviation.

[a]Mixed design.

2.9 | Method for addressing reporting biases

Egger´s and Begg´s tests were used for the main outcome to assess publication bias. Results of tests for funnel plot asymmetry were interpreted with visual inspection.

2.10 | Sensitivity analysis

Post hoc sensitivity analyses were performed excluding studies one by one from the global estimation for primary outcome (CAL change). Additionally, an overall visual distribution of the specific estimators of each publication was done, and any study following a different pattern was identified. Meta-analyses on CAL changes were also performed without those studies.

3 | RESULTS

3.1 | Study selection

Appendices S3 and S4 depict the study flow chart for both searches. For PICO #1, the electronic search yielded 870 titles and the manual search added 133 additional studies, with a total of 547 studies. After the review of full-text articles, 71 publications were excluded and 28 were included in the qualitative synthesis (agreement = 100.0%; kappa = 1; $p < 0.001$), representing 24 different studies. For PICO #2, the electronic search yielded 710 titles and the manual search added 22 additional studies. After the review of the full-text articles, 27 studies were excluded and 14 were included in the qualitative synthesis (agreement = 85.0%; kappa = 0.500; $p = 0.01$), representing 12 different studies. Excluded studies and reasons for exclusion are shown in Appendices S5 and S6, respectively.

Three sets of manuscripts reported different outcomes in different publications: Re et al. (2004) with Cardaropoli et al. (2004), Bayani et al. (2015) with Heravi et al. (2011a) and Zasčiurinskienė et al. (2018); Zasčiurinskienė, Lund, Lindsten, Jansson, and Bjerklin (2019a, 2019b).

3.2 | Study characteristics

Although the definition of the two PICO questions determined different populations, all the studies selected for PICO #2, except two (J. Lee, Miyazawa, et al., 2013; Ödman et al., 1994) were included in the first one. Therefore, results are presented together.

Table 2 depicts the methodological characteristics of the 26 included studies.

There were mainly case series with a pre–post-design (13 prospective and 4 retrospective), followed by RCTs (1 split mouth and 4 with parallel arms), three cohort studies (2 prospective and 1 retrospective) and one CCT (split mouth). Sixteen were done at university settings, 9 in private practices and 1 in combined settings, with funding being scarcely reported. Nearly half of them were done in Europe ($n = 12$), and the other were distributed by Asia ($n = 8$), America ($n = 4$) or Africa ($n = 2$). Overall study duration (i.e. baseline measurements to end of periodontal/orthodontic/combined treatment) varied from 6 months to nearly two years, with orthodontic therapy lasting from 3 to 36 months and at least 2 visits during the study (range: 2–6). There was only one study (Carvalho et al., 2018) comparing data from one cohort of patients with periodontitis ($n = 10$) versus one

Time pointsn (months)	Study groups	Author´s conclusion
2 (0; 30)	Non-Periodontitis	Adult patients exhibited greater crestal bone loss during treatment, but in the absence of compromising conditions (e.g. periodontitis) they are not more likely than adolescents to lose periodontal support
3 (0; DT; 16)	Non-Periodontitis	Preventive periodontal treatment before orthodontic manipulation might help to prevent periodontal destruction and plaque accumulation
2 (0; 12)	Non-Periodontitis	Treatment with fixed buccal orthodontic appliances was associated with a worsen periodontal condition when compared to treatment with removable aligners
2 (0; 9)	Non-Periodontitis	The periodontal biotype should be properly identified before orthodontic treatment to avoid the development of gingival recession
2 (0; 33.79)	Non-Periodontitis	The orthodontic tooth movement per se does not cause attachment loss. The mean individual bone losses of all interproximal surfaces in both groups did not reach statistical significance. There was no association observed between bone loss with any comorbidity factor

without periodontitis (n = 10); 20 studies dealt with participants with periodontitis and 5 with non-periodontitis patients.

3.3 | Participant's characteristics

3.3.1 | General characteristics

Table 3 presents information related to general characteristics of included participants. Overall, this review included data from 669 participants (438 with periodontitis and 231 without periodontitis), with ages that ranged from 18 to 60 years old, mainly women (n = 521) and non-smokers. In three studies, representing 33 patients, orthodontic therapy with TADs or implants was performed in all patients (skeletal anchorage). Ten studies mentioned different types of conventional anchorage, and two studies reported data from patients with TADs mixed with patients without TADs. Eleven studies did not report information about the anchorage used.

3.3.2 | Periodontal characteristics

Periodontal inclusion criteria (Table 4) showed a wide variation in their definitions. Non-periodontitis cases usually included periodontally healthy participants, although information regarding specific criteria was usually missing, except for the study of (Carvalho et al., 2018). Regarding periodontitis, the identified studies dealt with both patients presenting mainly localized intrabony defects (n = 10) and generalized periodontitis cases (n = 10).

Information on periodontal therapy is reported in Table 3. In non-periodontitis participants, professional mechanical plaque removal (PMPR) (Trombelli et al., 2015) and oral hygiene instructions (OHI) before orthodontic therapy were only reported in 3 studies (Carvalho et al., 2018; Karkhanechi et al., 2013; Sadiq & Badea, 2012). In periodontitis patients, scaling and root planing (SRP) with or without OHI and periodontal surgical procedures were usually performed. Surgeries included open flap debridement (OFD) (Cardaropoli et al., 2004; Corrente et al., 2003; Melsen et al., 1989; Re et al., 2000), modified Widman flaps (MWF) (Ogihara & Tarnow, 2015; Zasčiurinskienė et al., 2018, 2019a, 2019b), apically position flaps (APF) (Aimetti et al., 2020) or regenerative procedures with different materials including enamel matrix derivatives, membranes or bone grafts (Aimetti et al., 2020; Attia et al.,2012, 2019; Cardaropoli et al., 2006; Ghezzi et al., 2008; Ogihara & Tarnow, 2015; Ogihara & Wang, 2010). In one study (Attia et al., 2019), diode laser was additionally applied in adjunct with surgery.

In all studies dealing with periodontitis patients, periodontal therapy was done before the orthodontic treatment, except for one arm in the study from Zasčiurinskienė et al. (2018, 2019a, 2019b), where only PMPR was done before orthodontic therapy, and SRP and MWF were done during orthodontic therapy. There was one study (Melsen et al., 1989) in which curettage and surgery was performed during orthodontic therapy when needed. In the remaining studies, the interval between periodontal therapy and application of orthodontic forces varied from forces applied immediately (Attia et al.,2012, 2019; Ogihara & Wang, 2010), 1 to 2 weeks (Cardaropoli et al., 2004; Corrente et al., 2003; Eliasson et al., 1982; Melsen et al., 1989; Re et al., 2000), 1 to 2 months (Attia et al., 2012; Cardaropoli et al., 2006; Ghezzi et al., 2008; Ogihara & Tarnow, 2015) or 3 to 6 months after surgery (Aimetti et al., 2020; in one arm from Zasčiurinskienė et al., 2018, 2019a, 2019b; Zhang et al., 2017).

Periodontal maintenance, consisting on PMPR was usually performed during orthodontic therapy, with intervals that ranged from

TABLE 3 Characteristics of study arms and study sample of included studies

Study	Periodontal status	Anchorage	Population	Sample size calculation	n	Age (years)			Gender (females)	Smokers	Definition of smokers
						Mean	SD	Range	*n* (%)	*n*	
Carvalho (2018)	Non-Periodontitis	NR	Periodontally healthy patients	No	10	22.9	5.23	NR	8 (80%)	0	NR
	Periodontitis	NR	Aggressive periodontitis patients	No	10	25	5.22	NR	9 (90%)	0	NR
Brown (1973)	Periodontitis	Conventional	Severe periodontal disease patients who presented migration and inclination of a molar with a intrabony defect due to the absence of a mandibular posterior tooth	No	4	NR	NR	NR	4 (100%)	NR	NR
Eliasson (1982)	Periodontitis	NR	Severe periodontal disease patients and protrusion of upper incisors	No	20	NR	NR	27–54	11 (55%)	NR	NR
Melsen (1989)	Periodontitis	Conventional	Migration of anterior incisor with the need of intrusion	No	30	NR	NR	22–56	25 (83%)	NR	NR
Ödman et al., (1994)	Periodontitis	Skeletal	Patients with bone loss where implants where used as anchorage in different type of orthodontic movements	No	8	47	NR	17–64	6 (67%)	NR	NR
Re et al., (2000	Periodontitis	Conventional	Severe periodontal disease with PTM of anterior teeth	No	64	NR	NR	NR	NR	NR	NR
Corrente et al., (2003)	Periodontitis	Conventional	Intrusion in migrated upper central incisors with intrabony defects	No	10	NR	NR	33–53	8 (80%)	NR	NR
Cardaropoli et al. (2004, Re (2004)	Periodontitis	Conventional	Intrusion in migrated upper central incisors with intrabony defects	No	28	44.79	7.66	29–60	22 (79%)	NR	NR
Cardaropoli et al., (2006)	Periodontitis	Conventional	Migrated upper central incisors with an intrabony defect treated with GTR	No	3	NR	NR	NR	0 (0%)	0	NR
Ghezzi (2008)	Periodontitis	NR	PTM of an anterior teeth with an intrabony defect treated with GTR	No	14	NR	NR	>21	NR	0	NR
Ogihara (2010)	Periodontitis	Conventional	Chronic periodontitis patients with intrabony defects treated with GTR and requiring orthodontic extrusion due to restorative reasons.	No	24	50.5	11.5	NR	20 (83%)	NR	NR
Attia (2012)	Periodontitis	Conventional	Chronic periodontitis patients with at least three intrabony defects with GTR with immediate orthodontic therapy	No	15[a]	NR	NR	25–48	10 (67%)	0	NR
	Periodontitis	Conventional	Chronic periodontitis patients with at least three intrabony defects with GTR with delayed orthodontic therapy	No	15[a]	NR	NR	25–48	10 (67%)	0	NR
Lee et al., (2013)	Periodontitis	Skeletal	Overerupted molar		14	41.9	NR	22–60.4	12 (86%)	NR	NR

(Continues)

TABLE 3 (Continued)

Study	Periodontal status	Anchorage	Population	Sample size calculation	n	Age (years)			Gender (females)	Smokers	Definition of smokers
						Mean	SD	Range	*n* (%)	*n*	
Ghezzi (2013)	Periodontitis	NR	PTM of an anterior teeth with an intrabony defect treated with GTR	No	10	>21 years	NR	NR	6 (60%)	NR	NR
Heravi (2011), Bayani et al. (2015)	Periodontitis	Skeletal	Overerupted upper first molar	No	10	43.6	NR	25–57	10 (100%)	NR	NR
Cao et al., (2015)	Periodontitis	NR	Chronic periodontitis patients with horizontal bone loss at upper incisors that need intrusion	No	14	NR	NR	22–41	11 (79%)	0	NR
Ogihara (2015)	Periodontitis	Mixed	An intrabony defect treated with GTR (EMD+FDBA) that need extrusion due to a subgingival caries	No	25	52	9	NR	19 (76%)	0	NR
	Periodontitis	Mixed	An intrabony defect treated with GTR (EMD+DFDBA) that need extrusion due to a subgingival caries	No	24	51	11	NR	20 (83%)	0	NR
	Periodontitis	Mixed	An intrabony defect treated with GTR (EMD) that need extrusion due to a subgingival caries	No	25	50	5	NR	19 (76%)	0	NR
Zasčiurinskienė et al. (2018, 2019a, 2019b)	Periodontitis	Mixed	Periodontal disease patients with malocclusion with periodontal therapy performed during orthodontic therapy	Yes	25	47.31	1.62	NR	16 (64%)	1	<5cig/day
	Periodontitis	Mixed	Periodontal disease patients with malocclusion with periodontal therapy performed before orthodontic therapy	Yes	25	43.49	2.27	NR	19 (76%)	1	<5cig/day
Zhang (2017)	Periodontitis	NR	Mild-to-severe periodontal disease patients with PTM	No	59	36.5	5.8	NR	21 (36%)	NR	NR
Attia (2019)	Periodontitis	Conventional	Patients with 2 contra-lateral intrabony defect treated with GTR and laser	Yes	15[a]	NR	NR	25–37	11 (73%)	0	NR
	Periodontitis	Conventional	Patients with 2 contra-lateral intrabony defect treated with GTR (without laser)	Yes	15[a]	NR	NR	25–37	11 (73%)	0	NR
Aimetti (2020)	Periodontitis	Conventional	Severe periodontal disease and PTM	No	21	52.6	5.9	44–68	16 (76%)	3	4 to 6 cig/day
Harris (1990)	Non-Periodontitis	NR	Periodontally healthy adults	No	122	27.9	5.3	20 – 40	122 (100%)	NR	NR
Sadiq (2008)	Non-Periodontitis	NR	Periodontally healthy adults and adolescents	No	14	25	NR	NR	10 (71%)	NR	NR

(Continues)

TABLE 3 (Continued)

Study	Periodontal status	Anchorage	Population	Sample size calculation	n	Age (years) Mean	SD	Range	Gender (females) n (%)	Smokers n	Definition of smokers
Karkhanechi et al., (2013)	Non-Periodontitis	NR	Periodontally healthy adults treated with fixed appliances	No	18	3.6	7.18	18 – 44	16 (89%)	0	NR
	Non-Periodontitis	NR	Periodontally healthy adults treated with removable aligners	No	17	28.6	6.86	18 – 44	12 (71%)	0	NR
Rasperini (2017)	Non-Periodontitis	NR	Periodontally healthy adults	No	16	21	8.2	NR	6 (38%)	0	NR
Zoizner (2018)	Non-Periodontitis	NR	Periodontally healthy adults	Yes	34	25.6	7.3	NR	10 (29.4%)	NR	NR

Abbreviations: AAP, American Academy of Periodontology; BOP, bleeding on probing; CAL, clinical attachment level; cig, cigarette; CS, coronal scaling; d, days; DFDBA, demineralized freeze-dried bone allograft; EMD, enamel matrix derivative; FMPS, full-mouth plaque score; GTR, guided tissue regeneration; mg, milligrams; mm, millimetres; m, months; MWF, Modified Widman flap; NA, not applicable; NR, not reported; OA, occlusal adjustment; OF, open flap; OHI, oral hygiene instructions; PPD, probing pocket depth; PMPR, professional mechanical plaque removal; PTM, pathologic tooth migration; RBL, radiographic bone loss; SRG, surgery; SRP, scaling and root planing; w, week; y, year.

[a]Split mouth.

1 to 6 months. Information regarding self-performed plaque control was reported in the included studies was scarce.

3.3.3 | Orthodontic characteristics

Orthodontic data, including inclusion criteria and type of appliance, are reported in Table 5. Mean treatment duration ranged from 1 month (Ogihara & Tarnow, 2015; Ogihara & Wang, 2010), where limited extrusion of one tooth was performed, to 33 months (Zoizner et al., 2018), for comprehensive orthodontic therapy. In general, treatment duration was shorter in studies with periodontitis patients compared to non-periodontitis patients. In three studies, the duration of the treatment was not reported (Attia et al.,,2012, 2019; Ghezzi et al., 2008). Considering the type of anchorage, in the skeletal anchorage group, the duration varied between 17 months for osseointegrated implants (Ödman et al., 1994), in which different types of movements were achieved, to 11.9 (Lee et al., 2013) and 7.7 months (Heravi et al., 2011a) for the TADs group, in which one molar was intruded. In the conventional anchorage group, treatment time ranged from 3 months for molar uprighting (Brown, 1973) to 18.6 months (Aimetti et al., 2020) for alignment and intrusion of the incisors. Initial malocclusions and treatment scope for the included studies are described in Table 5. For analytical purposes, those studies in which the intrusion or extrusion was the main treatment goal were selected and included for subgroup analysis. Fixed appliances were used in all the studies, since this was one of our inclusion criteria. Two of them compared fixed versus functional appliances (Zhang et al., 2017) or aligners (Karkhanechi et al., 2013). According to the description of anchorage, skeletal group comprised 22 osseointegrated implants used as orthodontic anchorage in eight partially edentulous adult patients (Ödman et al., 1994) and 36 TADs placed in 24 patients: 22 TADs in 10 patients (Heravi et al., 2011a) and 14 TADs in 14 patients (S. J. Lee, Miyazawa, et al., 2013). Loading protocol, type of anchorage applied, length and number of implants per patient are shown in Table 5. Conventional anchorage was used in 9 studies. Most of them used sectionals connecting posterior teeth alone (Brown, 1973), combined with palatal bars (Corrente et al., 2003) (Cardaropoli et al., 2004), labial arches (Attia et al., 2012, 2019) or both appliances (Re et al., 2000). There were two studies (Cardaropoli et al., 2006) (Aimetti et al., 2020) in which cantilevers were used. In one study (Melsen et al., 1989), 4 different groups were defined according to the type of anchorage used for incisors intrusion.

3.4 | Study outcomes

Information on the reported outcomes is presented in Appendix S7.

Periodontal measurements included CAL, probing pocket depth (PPD), recession (REC), plaque indices (PI), gingival indices (GI), bleeding on probing (BOP) and radiographic bone levels (RBL); either in a full-mouth approach or only in the targeted teeth (teeth

with intrabony defects and/or teeth with malpositions). Plaque levels, BOP, GI or REC were scarcely reported, while CAL, PPD or RBL were given in the majority of publications except for Ödman et al. (1994) (Ödman et al., 1994) and Lee, Miyazawa, et al. (2013) (J. Lee, Miyazawa, et al., 2013), as they were studies coming from PICO #2. Intraoral radiographs were the preferred method to determine bone levels (either in mm or in %), except for two studies (Cao et al., 2015; Zasčiurinskienė et al., 2018, 2019a, 2019b), in which CBCT measurements were used. The timing to register periodontal outcomes in baseline could be either before or after periodontal treatment was finished, while second visits varied from 3 to 30 months after baseline.

Orthodontic outcomes were scarcely reported, being the type and amount of tooth movement the most common one. Two studies reported changes in tooth position (mm) in 3D (J. Lee, Miyazawa, et al., 2013; Ödman et al., 1994), while Corrente et al. (2003) (Corrente et al., 2003) and Cardaropoli et al. (2004) (Cardaropoli et al., 2004) reported intrusion only of the incisors (mm), and in one study (Harris & Baker, 1990), intrusion in molars was reported. The second most commonly reported outcome was root resorption. One study registered patient-reported outcomes measurements (PROMS) related to TADs (Heravi et al., 2011a), and there was one study in which the levels of inflammatory cytokines were reported (Zhang et al., 2017).

3.5 | Main effects

3.5.1 | Periodontal effects

Results from meta-analyses on periodontal outcomes are reported in Table 6. Appendices S8–S10 show the forest plots for CAL, PPD and BOP changes (n of studies = n_s; n of patients = n_p).

In patients without periodontitis, changes in CAL (mm) (n_s = 2; n_p = 26; ME = 0.079; 95% CI [−0.011; 0.168]; p = 0.085), PPD (mm) (n_s = 2; n_p = 26; ME = 0.313; 95% CI [−0.079; 0.705]; p = 0.117) and BOP (%) (n_s = 2; n_p = 26; ME = 3.631; 95% CI [−2.108; 9.370]; p = 0.215) were minimal and non-statistically significant through time (p > 0.05), although a slight loss in RBL (mm) could be observed based in one study (n_s = 1; n_p = 122; ME = −0.400; 95% CI [−0.579; −0.221]; p < 0.001).

In patients with treated periodontitis whose baseline measurements were given after periodontal therapy had finished, no significant changes were observed in CAL (mm) (n_s = 5; n_p = 69; ME = 0.002; 95% CI [−0.286; 0.289]; p = 0.990) or BOP (%) (n_s = 3; n_p = 41; ME = 0.961; 95% CI [−0.774; 2.695]; p = 0.278), with a slight PPD reduction (mm) (n_s = 6; n_p = 89; ME = 0.125; 95% CI [0.052; 0.197]; p < 0.001) and greater RBL gain (mm) (n_s = 2; n_p = 24; ME = 0.893; 95% CI [0.357; 1.428]; p < 0.001), during orthodontic therapy.

By contrast, in periodontitis patients whose baseline measurements were reported before periodontal therapy, a significant gain in CAL (mm) (n_s = 11; n_p = 214; ME = 3.523; 95% CI [2.353; 4.693]; p < 0.001) and in RBL (mm) (n_s = 7; n_p = 137; ME = 2.366; 95% CI [1.118; 3.613]; p < 0.001), while a reduction in PPD (mm) (n_s = 12; n_p = 302; ME = 3.466; 95% CI [2.630; 4.303]; p < 0.001) and in BOP (%) (n_s = 4; n_p = 138; ME = 26.138; 95% CI [1.306; 50.970]; p = 0.039) was observed after both treatments were done.

No significant changes in REC were observed in any study groups, although patients with periodontitis with measurements before periodontal therapy tended to have higher increases in REC compared with the other groups.

Subgroup analyses could only be done in those studies reporting periodontitis patients with baseline information before periodontal and orthodontic therapy. Their results are reported in Table 7.

Considering the type of surgery, patients that had received periodontal regenerative surgeries before orthodontic therapy, reported higher gains in RBL than non-regenerative surgeries, although similar CAL and PPD changes were observed. One study (Zasčiurinskienė et al., 2018, 2019a, 2019b) reported surgeries performed during orthodontic therapy, and their results were the lowest in terms of RBL (ME = 0.020; 95% CI [−0.019; 0.059]; p = 0.317) and CAL (ME = 0.440; 95% CI [0.264; 0.616]; p < 0.001) changes, mainly due to methodological differences (general vs local location, resective vs regenerative surgeries).

Regarding the interval between periodontal and orthodontic therapy, the worst results in terms of CAL, PPD or RBL changes were observed when orthodontic forces were applied 3 to 6 months after periodontal therapy, although these results came from only one study (Zasčiurinskienė et al., 2018, 2019a, 2019b). Similar values were observed for intervals of 1 to 2 months or less than 2 weeks.

Regarding the orthodontic movements, similar results were obtained for intrusive and extrusive movements in terms of CAL or PPD changes. However, in the extrusive movements (n_s = 3; n_p = 74; ME = 4.00; 95% CI [3.236; 4.763]; p > 0.001) there was greater RBL gain (mm) than in the intrusive ones (n_s = 3; n_p = 38; ME = 1.36; 95% CI [0.004; 2.717]; p = 0.049).

Regarding the type of anchorage (conventional, skeletal or NR [when no additional conventional devices were specified]), the highest CAL (mm) gain was observed for conventional anchorage (n_s = 5; n_p = 80; ME = 4.569; 95% CI [3.493; 5.645]; p < 0.001) and significant PPD reductions that ranged between 2.4 and 3.9 mm were observed in the three subgroups (Table 7).

3.5.2 | Orthodontic effects

Table 5 shows the results of orthodontic outcomes. No meta-analysis could be performed with these variables. OTM was reported in the only study that used osseointegrated implants (Ödman et al., 1994), in which a mean movement of 3.9 mm (range 0.6 to 7 mm) was observed. In the studies in which TADs were used (Heravi et al., 2011b; S. J. Lee, Miyazawa, et al., 2013), a mean molar intrusion of 2.1 mm ([SD = 0.9 mm]; p = 0.001) and 1.35 mm ([SD: 0.48 mm]; $p \leq 0.001$) was achieved, respectively.

In the conventional anchorage group, the intrusion movement was the only variable reported, ranging from 1.95 mm (SD = 0.48)

TABLE 4 Data of the periodontal inclusion criteria and periodontal treatment performed in the included studies

Study	Periodontal groups	Periodontal criteria: Inclusion criteria	Periodontal treatment duration: Months	Non surgical professional periodontal treatment (PMPR, SRP): Before the study
Carvalho (2018)	Non-periodontitis	1) PPD and CAL <3 mm 2) BOP < 10%	NR	PMPR +OHI
	Periodontitis	Aggressive periodontitis (1999 AAP criteria)	NR	SRP +OHI + antibiotic (metronidazole 250 mg +amoxicillin 500 mg)
Brown (1973)	Periodontitis	1) Severe periodontitis 2) Intrabony defect at mesial aspect of a posterior lower molar	NR	SRP
Eliasson (1982)	Periodontitis	1) Severe periodontitis 2) Gingival inflammation 3) Alveolar bone loss	(4–6)	SRP
Melsen (1989)	Periodontitis	Alveolar bone loss	NR	curettage
Ödman et al., (1994)	Periodontitis	Alveolar bone loss	NR	NR
Re et al., (2000	Periodontitis	Severe periodontitis	NR	SRP
Corrente et al., (2003)	Periodontitis	1) Intrabony defect at mesial aspect of a extruded incisor with PPD ≥6 mm 2) FMPS ≤15%	NR	SRP
Cardaropoli et al. (2004, Re (2004)	Periodontitis	Chronic periodontitis with: 1) 1 upper central incisor extruded 2) Intrabony defect at mesial aspect of a extruded incisor with PPD ≥6 mm 3) PL ≤15%	NR	SRP
Cardaropoli et al., (2006)	Periodontitis	1) PTM 2) Intrabony defect on an upper central incisor with PPD ≥6 mm 3) FMPS ≤15%	NR	SRP
Ghezzi (2008)	Periodontitis	1) PTM 2) Severe periodontitis 3) Intrabony defect with PD ≥6 mm 3) FMPS and FMBS <25%	NR	SRP
Ogihara (2010)	Periodontitis	Chronic periodontitis with a intrabony defect of >6 mm at one or two sites	12	SRP +OHI
Attia (2012)	Periodontitis	Chronic periodontitis with at least 3 intrabony defects with PPD >5 mm	NR	SRP
Lee et al., (2013)	Periodontitis	30% to 50% horizontal bone loss of a over erupted molar with a healthy periodontal condition	NR	NR
Ghezzi (2013)	Periodontitis	1) PTM 2) Periodontal disease	NR	SRP
Heravi (2011), Bayani et al. (2015)	Periodontitis	1) Alveolar bone loss 2) No active periodontal disease	NR	NR
Cao et al., (2015)	Periodontitis	Chronic periodontitis with: 1) FMPS ≤15% 2) BOP <25% 3) Horizontal bone defects	NR	SRP +OHI

Surgical professional periodontal treatment (type of surgery)	Supportive periodontal therapy	Self-performed plaque control	Other treatments	Timing
Before the study	During the study (months interval)	During the study	During the Study	Interval between periodontal and orthodontic therapy
NR	CS +OHI (1)	NR	NR	NR
NR	CS +OHI (6)	NR	NR	NR
NR	NR	NR	NR	NR
NR	NR	NR	NR	NR
OF (before and during ortho)	Curettage (when needed)	NR	NR	1 w after SRG
NR	NR	NR	NR	NR
OF	PMPR (2–3)	NR	NR	1 w after periodontal treatment
OF	PMPR (2–3)	NR	NR	7–10 d after SRG
OF	PMPR (3–4)	NR	NR	7–10 d after SRG
GTR (collagen bovine bone graft)	PMPR (3)	NR	NR	2 w after SRG
GTR (EMD or collagen membrane +bone graft)	SRP+OHI (1)	NR	NR	1 y after SRG
GTR (EMD +DFDBA)	CS (NR)	NR	NR	1 m after SRG
GTR (bioactive glass +collagen membrane)	PMPR +OHI (1)	NR	NR	Immediately after SRG 2 m after SRG
NR	Yes NR	NR	NR	NR
GTR (collagen bone graft +EMD)	NR	NR	NR	1 m after SRG
NR	OHI	NR	NR	NR
NR	CS (3)	NR	Fibrotomy	NR

(Continues)

TABLE 4 (Continued)

Study	Periodontal groups	Periodontal criteria Inclusion criteria	Periodontal treatment duration Months	Non surgical professional periodontal treatment (PMPR, SRP) Before the study
Ogihara (2015)	Periodontitis	1) CAL ≥6 mm 2) RBL 3) 1 intrabony defect	NR	SRP +OHI + OA
Zasčiurinskienė et al. (2018, 2019a, 2019b)	Periodontitis	1) RBL ≥3 teeth and more than 1/3 of the root length 2) ≥3 teeth with BOP, PPD ≥4 mm and CAL ≥4 mm	1.38 (0.18) 4.56 (0.35)	PMPR (before ortho) SRP (during ortho) PMPR +SRP
Zhang (2017)	Periodontitis	1) PTM 2) BOP 3) CAL 1–2 mm, 3–4 mm or ≥5 mm	NR	CS +SRP + OHI
Attia (2019)		1) Interproximal bone loss 2) Two intrabony defects in premolar/molar region with CAL and PPD >5 mm	NR	SRP +OHI
Aimetti (2020)	Periodontitis	Severe chronic periodontitis with: 1) ≥4 sites in at least six anterior teeth with CAL and PPD ≥8 mm 2) PTM	6	SRP
Harris (1990)	Non-periodontitis	NR (indirect information from tables)	NR	NR
Sadiq (2008)	Non-Periodontitis	NR (indirect information from tables)	NR	PMPR
Karkhanechi et al., (2013)	Non-periodontitis	No CAL loss	NR	PMPR +OHI
Rasperini (2017)	Non-periodontitis	1) No history of periodontal treatment 2) No gingival recession	NR	NR
Zoizner (2018)	Non-Periodontitis	NR (indirect information from tables)	NR	NR

Abbreviations: AAP, American Academy of Periodontology; BOP, bleeding on probing; CAL, clinical attachment level; CS, coronal scaling; d, days; DFDBA, demineralized freeze-dried bone allograft; EMD, enamel matrix derivative; FMPS, full-mouth plaque score; GTR, guided tissue regeneration; mg, milligrams; mm, millimetres; m, months; MWF, Modified Widman flap; NA, not applicable; NR, not reported; OA, occlusal adjustment; OF, open flap; OHI, oral hygiene instruction; PMPR, professional mechanical plaque removal; PPD, probing pocket depth; PTM, pathologic tooth migration; RBL, radiographic bone loss; SRG, surgery; SRP, scaling and root planing; w, week; y, year.

(Cardaropoli et al., 2004) to 2.1 mm ([SD = 0.5 mm]; $p \leq 0.001$) (Corrente et al., 2003).

Root resorption after the orthodontic treatment in periodontitis patients was reported in a few studies of both anchorage groups. In the conventional anchorage group, Melsen et al. (1989) found 1 to 3 mm of root resorption in the treated incisors, while Corrente et al. (2003) reported no resorption of the orthodontically intruded ones. In the skeletal anchorage group, only one study observed apical root resorption (Heravi et al., 2011a) that ranged from 0.2 to 0.4 mm. On the other hand, in healthy patients treated orthodontically, root resorption was also observed. Harris et al. (1990) (Harris & Baker, 1990) found 1 to 1.5 mm of root resorption and (Zasčiurinskienė et al., 2018, 2019a, 2019b) found 1.1 to 1.26 mm.

In one study (Melsen et al., 1989), crown length variation (from the incisal edge to the most apical margin of the gingiva at the level of the intruded incisors) was reported (mean = 1.08 mm; SD = 1.14 mm).

No information of tooth mobility, tooth loss or implant-related outcomes (rate of failure, loss of anchorage) was reported in any of the included studies.

Surgical professional periodontal treatment (type of surgery)	Supportive periodontal therapy	Self-performed plaque control	Other treatments	Timing
Before the study	During the study (months interval)	During the study	During the Study	Interval between periodontal and orthodontic therapy
GTR (EMD +DFDBA) GTR (EMD +DFDBA) GTR (EMD)	CS +OHI (6)	NR	Forced eruption to establish 2 mm biologic width	1 m after SRG 1 m after SRG 1 m after SRG
MWF during ortho MWF before ortho	PMPR (3–6)	NR	NR	Simultaneous perio and ortho treatment 3–6 m after SRP or SRP +SRG
Yes NR	NR	NR	Subgingival irrigation with chlorhexidine	6 m after SRG
GTR (bioactive glass graft +collagen membrane +diode laser) GTR (bioactive glass graft +collagen membrane)	NR	Tooth brushing	NR NR	Immediately after SRG Immediately after SRG
APF or GTR (EMD alone or EMD +bone graft)	PMPR	NR	NR	6 m after SRG
NR	NR	NR	NR	NA
NR	NR	NR	NR	NA
NR	NR	NR	NR	NA
NR	NR	NR	NR	NR
NR	NR	NR	NR	NA

3.6 | Assessment of risk of bias

The overall quality of the included studies was evaluated as 'low'. Considering the 17 pre–post-intervention studies assessed, none of them was rated as 'good' quality. Eight of them were rated as 'fair' (moderate risk of bias), and nine were rated as 'poor' (Appendix S11). According to the NOS scale for cohort studies, three out of three studies (2 prospective and 1 retrospective) were rated as 'fair' quality (Appendix S12). The only study rated according to ROBINS-I tool, received an overall assessment of 'serious' risk of bias. Detailed information about each specific domain and complete evaluation can be seen in Appendix S13. The five RCTs included in this review were assessed using ROB 2.0 tool (Appendix S14). After evaluating the five domains, the overall bias assessment was 'high' for one RCT; two RCTs were rated as 'low risk of bias'; and another two were rated with 'some concern'.

3.7 | Publication bias

Begg´s test for small-study effects and Egger's linear regression test, performed for CAL change, showed evidence of publication

TABLE 5 Data of the orthodontic characteristics, movements and description of the anchorage system in the included studies

Study	Periodontal groups	Orthodontic duration (months) mean (SD) [range]	Timing: Intervals between treatment phases (perio previous ortho)	Orthodontic baseline malocclusion	Treatment scope	Type of appliances	Anchorage	
							Conventional or not conventional	Type
Carvalho (2018)	Non-Periodontitis	18.9 (0.99)	NR	NR	Intrusion and alignment	Edgewise brackets	NR	NR
	Periodontitis	16 (1.56)	NR	PTM	Intrusion and alignment	Edgewise brackets	NR	NR
Brown (1973)	Periodontitis	[3–4]	NR	Migration and mesial inclination of the lower molar into the edentulous space	Molar Uprighting	Edgewise brackets Sectional arch	Conventional	Sectional arch
Eliasson (1982)	Periodontitis	[4–16]	NR	Protrusion and diastema of upper incisors	Incisor retrusion	Removable appliances	NR	NR
Melsen (1989)	Periodontitis	[6–18]	1 w after SRG	PTM of incisor with OB and OJ	Intrusion and alignment	Edgewise J Hook Utility arches with high-pull Intrusion bent into a loop Intrusive arches	Conventional	J Hook and high-pull headgear Palatal arch
Ödman et al., (1994)	Periodontitis	17 [4–33]	NR	Malocclusion: deep/open/ cross bite, rotation, crowding, inclination of upper molar	In/Extrusion, alignment, tipping, rotation, bodily and torquing movement	Edgewise brackets	Skeletal	Implants
Re et al., (2000)	Periodontitis	10 (3.04) [3–18]	1w after periodontal treatment	PTM with malocclusion	Intrusion and alignment	Fixed appliances sectional arch/ intrusive arch	Conventional	Lingual or a palatal arch posterior segments
Corrente et al., (2003)	Periodontitis	10 (2.6)	7–10 d after SRG	Migration and extrusion of the upper anterior teeth	Intrusion and alignment	Fixed appliances intrusion arches and cantilevers	Conventional	Palatal arche segments
Cardaropoli et al. (2004 Re (2004)	Periodontitis	11.71 (2.98)	7–10 d after SRG	Migration and extrusion of an upper incisor and diastema	Intrusion and alignment	Fixed appliances sectional arches and cantilevers	Conventional	Palatal arche posterior segments

Not conventional					Orthodontic outcomes			
					Orthodontic index			
Loading protocol	Type of anchorage	Implants/ screws: Location	Implants / screws: Number	Implants/ screw length and diameter	Index	Changes baseline-post-orthodontic visit n, mean (SD), p-value	Root resorption	Other variables assessed
NR	NR	NR	NR	NR	NR	NR	NR	NR
NR	NR	NR	NR	NR	NR	NR	NR	NR
NA	NA	NA	NA	NA	NR	NR	NR	Histologic examination
NR	NR	NR	NR	NR	NR	NR	NR	NR
NA	NA	NA	NA	NA	Clinical crown length (mm)	30, 1.08 (1.14), NR	1–3 mm in all cases	Visual inspection of gingival health
Delayed (3–9 m)	Direct	Multiple. At level of tooth: 14, 15, 16, 23, 24, 25, 35, 36, 37, 45, 46	1, 2 or 3 per patient	Multiple: 7,10,15 mm length Diameter NR	Tooth movement[c]	9z-axis: −0.82 (1.7) 2D: 3.05 (1.5) 3D: 3.9 (1.74)	NR	NR
NA	NA	NA	NA	NA	NR	NR	NR	Pulp vitality alteration: none Compensatory extrusion of the neighbouring teeth: none
NA	NA	NA	NA	NA	Intrusion (mm)	10, 2.1 (0.5), NR	None	Papilla index
NA	NA	NA	NA	NA	Intrusion (mm)	28, 1.95 (0.48), NR	NR	Papilla index

(Continues)

TABLE 5 (Continued)

Study	Periodontal groups	Orthodontic duration (months) mean (SD) [range]	Timing: Intervals between treatment phases (perio previous ortho)	Orthodontic baseline malocclusion	Treatment scope	Type of appliances	Anchorage	
							Conventional or not conventional	Type
Cardaropoli et al., (2006)	Periodontitis	[4–9]	2 w after SRG	PTM with flared anterior teeth	Intrusion and alignment	Fixed appliances intrusion arches and cantilevers Utility arch	Conventional	Cantilevers
Ghezzi (2008)	Periodontitis	NR	1y after SRG	Migration and diastema	Alignment and intrusion	Fixed appliances	NR	NR
Ogihara (2010)	Periodontitis	1	1 m after SRG	NR	Extrusion	Fixed appliances	Conventional	Occlusal metal bar
Attia (2012) (Immediate otho)	Periodontitis	NR[a]	Immediately after GTR	Migration, extrusion and malocclusion	Intrusion and alignment	Fixed appliances sectional arch	Conventional	Labial arch posterior segment
Attia (2012) (Delayed ortho)	Periodontitis	NR[a]	2 m after GTR	Migration, extrusion and malocclusion	Intrusion and alignment	Fixed appliances sectional arch	Conventional	Labial arch posterior segment
Lee et al., (2013)	Periodontitis	11.9 [5–20]	NR	Overerupted molar	Intrusion	Partially fixed edgewise appliance	Skeletal	Microscrew
Ghezzi (2013)	Periodontitis	9 (3.2)	1 m after SRG	PTM	Intrusion and alignment	Fixed appliances (self-ligation bracket)	NR	NR
Heravi (2011), Bayani et al. (2015)	Periodontitis	7.7 [4.3 – 11.5]	NR	Overerupted upper first molar	Molar Intrusion	Molar bands TMA spring	Skeletal	Microscrew
Cao et al., (2015)	Periodontitis	19	NR	Migration and extrusion of upper anterior teeth	Intrusion and alignment	Fixed appliances Utility arch	NR	NR
Ogihara (2015) (EMD+FDBA)	Periodontitis	1	1 m after SRG	Need to extrusion due for subgingival caries	Extrusion	Fixed appliance occlusal metal bar	Mixed	Occlusal metal bar Microscrew
Ogihara (2015) (EMD+DFDBA)	Periodontitis	1	1 m after SRG	Need to extrusion due for subgingival caries	Extrusion	Fixed appliance occlusal metal bar	Mixed	Occlusal metal bar Microscrew
Ogihara (2015) (EMD)	Periodontitis	1	1 m after SRG	Need to extrusion due for subgingival caries	Extrusion	Fixed appliance occlusal metal bar	Mixed	Occlusal metal bar Microscrew

(Continues)

Not conventional					Orthodontic outcomes			
					Orthodontic index			
Loading protocol	Type of anchorage	Implants/ screws: Location	Implants / screws: Number	Implants/ screw length and diameter	Index	Changes baseline-post-orthodontic visit n, mean (SD), p-value	Root resorption	Other variables assessed
NA	NA	NA	NA	NA	NR	NR	NR	NR
NA	NA	NA	NA	NA	NR	NR	NR	NR
NA	NA	NA	NA	NA	NR	NR	NR	NR
NA	NA	NA	NA	NA	NR	NR	NR	NR
NA	NA	NA	NA	NA	NR	NR	NR	NR
NR	Indirect	Buccal	1	1.2 mm diameter 6 mm length	Tooth movement*d*	14 1.35 (0.48)	NR	NR
NR	NR	NR	NR	NR	NR	NR	NR	NR
Delayed (2 w)	Direct	First upper molar (buccal & palatal)	2	1,33 diameter 7 mm length	Intrusion (mm)	102.1 (0.9)	Molar roots: Pa: 0.2 (0.2) Me:0.4 (0.3) Di: 0.2 (0.3)	Patients perception: Tongue irritation symptoms
NR	NR	NR	NR	NR	NR	NR	NR	NR
NR	NR	NR	NR	NR	NR	NR	NR	NR
NR	NR	NR	NR	NR	NR	NR	NR	NR
NR	NR	NR	NR	NR	NR	NR	NR	NR

TABLE 5 (Continued)

Study	Periodontal groups	Orthodontic duration (months) mean (SD) [range]	Timing: Intervals between treatment phases (perio previous ortho)	Orthodontic baseline malocclusion	Treatment scope	Type of appliances	Anchorage	
							Conventional or not conventional	Type
Zasčiurinskienė et al. (2018, 2019a, 2019b) (Test)	Periodontitis	20.30 (1.22)	Simultaneous perio and ortho treatment	Malocclusion and flared incisors	Intrusion and alignment	Fixed appliances (self-ligation bracket)	Mixed	Yes/NR Microscrew or implants (temporary crown)
Zasčiurinskienė et al. (2018, 2019a, 2019b) (Control)	Periodontitis	21.17 (0.88)	3–6 m after SRP or SRP+SRG	Malocclusion and flared incisors	Intrusion and alignment	Fixed appliances (self-ligation bracket)	Mixed	Yes/NR Microscrew or implants (temporary crown)
Zhang (2017)	Periodontitis	6	6 m after SRG	PTM	Intrusion and alignment	Functional Fixed appliances	NR	NR
Attia (2019) (Laser)	Periodontitis	NR[b]	Immediately after GTR	Migration or crowding of anterior teeth	Intrusion and alignment	Fixed appliances sectional arch	Conventional	Labial arch posterior segment
Attia (2019) (No laser)	Periodontitis	NR[b]	Immediately after GTR	Migration or crowding of anterior teeth	Intrusion and alignment	Fixed appliances sectional arch	Conventional	Labial arch posterior segment
Aimetti (2020)	Periodontitis	18.6 (9) [4 – 36]	6 m	PTM of upper and/or lower anterior teeth	Intrusion and alignment	Fixed appliances Cantilever	Conventional	Cantilever
Harris (1990)	Non-Periodontitis	30 (4.2)	NA	Malocclusion: Class II div.1	Alignment	Fixed appliances (Edgewise brackets)	NR	NR
Sadiq (2008)	Non-Periodontitis	16 (4.2)	NA	NR	NR	Fixed appliances	NR	NR
Karkhanechi et al., (2013) (Fixed appliance)	Non-Periodontitis	12	NA	NR	NR	Fixed appliances	NR	NR
Karkhanechi et al., (2013) (Removable aligners)	Non-Periodontitis	12	NA	NR	NR	Aligners	NR	NR
Rasperini (2017)	Non-Periodontitis	9	NA	NR	Alignment	Fixed appliances	NR	NR
Zoizner (2018)	Non-Periodontitis	33.79 (15.97)	NA	NR	Alignment	Fixed appliances	NR	NR

Abbreviations: d, day; Di, distal; div, division; mm, millimetres. m, month; Me, mesial; NA, not applicable; NR, not reported; OB, overbite; OJ, overjet; Pa, palatal; PM, premolars; PTM, pathological tooth migration; SRG, Surgery; SRP, scaling and root planing; TMA, titanium molybdenum alloy; w, week; y, year.

[a]Outcomes recorded during orthodontic treatment at 12 months

[b]Outcomes recorded during orthodontic treatment at 9 months

[c]z-axis: intrusion (mm), x-y-axis (2D), x-y-z-axis (3D)

[d]Z: intrusive (+) and (-) extrusive movements, X: distobuccal changes, Y: mesiodistal changes

					Orthodontic outcomes			
Not conventional					Orthodontic index			
Loading protocol	Type of anchorage	Implants/ screws: Location	Implants / screws: Number	Implants/ screw length and diameter	Index	Changes baseline-post-orthodontic visit n, mean (SD), p-value	Root resorption	Other variables assessed
NR	Direct & indirect	NR	NR	NR	Angle class	NR	1.10 (0.94 – 1.28)	NR
NR	Direct & indirect	NR	NR	NR	Angle class	NR	1.26 (1.07 – 1.46)	NR
NR	NR	NR	NR	NR	NR	NR	NR	Cytokines (IL–1b, 5, 6, 8; TNFx; PGE2; hs-CRP)
NA	NA	NA	NA	NA	NR	NR	NR	NR
NA	NA	NA	NA	NA	NR	NR	NR	NR
NA	NA	NA	NA	NA	NR	NR	NR	NR
NR	NR	NR	NR	NR	NR	NR	1.0 – 1.5 mm of root length	Teeth erosion
NR	NR	NR	NR	NR	NR	NR	NR	NR
NR	NR	NR	NR	NR	NR	NR	NR	NR
NR	NR	NR	NR	NR	NR	NR	NR	NR
NR	NR	NR	NR	NR	NR	NR	NR	Periodontal biotype
NR	NR	NR	NR	NR	NR	NR	NR	NR

TABLE 6 Results of the meta-analyses for the primary and secondary periodontal outcomes of orthodontic tooth movement

	Periodontal diagnoses	Time of Perio Outcomes collection	*n* study	*n* patients	ME	95% CI		95% PI		*p*-value	I^2	*p*-value
						Lower	Upper	Lower	Upper			
CAL changes (mm)	Non-periodontitis		2	26	0.08	−0.01	0.17	NA	NA	0.085	0	<0.001
	Periodontitis	After	5	69	0.01	−0.29	0.29	−1.02	1.03	0.990	77.3	0.001
		Before	11	214	3.52	2.35	4.69	−1.10	8.15	<0.001	99.3	<0.001
PPD changes (mm)	Non-periodontitis		2	26	0.31	−0.08	0.70	NA	0.23	0.117	96.1	<0.001
	Periodontitis	After	6	89	0.12	0.05	0.19	0.02	6.75	<0.001	0.0	0.424
		Before	12	302	3.47	2.63	4.30	0.18	NA	<0.001	98.6	<0.001
RBL changes (mm)	Non-periodontitis		1	122	−0.40	−0.58	−0.22	NA	6.95	<0.001		
	Periodontitis	After	3	49	0.51	−0.07	1.25	−7.39	8.57	0.001	85.9	0.001
		Before	6	112	2.76	0.77	4.74	−4.63	10.14	<0.001	100.0	<0.001
BOP changes (%)	Non-periodontitis		2	26	3.63	−2.11	9.37	NA	NA	0.215	80.2	0.025
	Periodontitis	After	3	41	0.96	−0.77	2.69	−18.78	NA	0.278	73.0	0.024
		Before	4	138	26.14	1.31	50.97	−95.68	NA	0.039	99.9	<0.001
REC changes (mm)	Non-periodontitis		2	26	0.23	−0,32	0.77	NA	1.03	0.418	79.1	0.029
	Periodontitis	After	2	31	0.08	−0.37	0.53	NA	8.15	0.731	0	0.909
		Before	2	38	1.41	−0.16	2.98	NA	NA	0.079	0	0.594

Abbreviations: BOP, bleeding on probing; CAL, clinical attachment level; CI, confidence interval; I2, heterogeneity; ME, mean effect; mm, millimetres; PPD, probing pocket depth; RBL, radiographic bone loss; REC, recession.

TABLE 7 Results of the subgroup meta-analyses for the primary and secondary periodontal outcomes in studies reporting a combined periodontal and orthodontic treatment (baseline before periodontal therapy)

						95% CI		95% PI				
Outcomes	**Subgroups**	**Categories**	***n* study**	***n* patients**	**ME**	**Lower**	**Upper**	**Lower**	**Upper**	***p***	I^2	***p***
CAL changes (mm)	Overall		11	214	3.52	2.35	4.69	−1.10	8.15	<0.001	99.3	<0.001
	Interval periodontal & orthodontic therapy	≤2 weeks	5	81	3.89	1.73	6.05	−4.15	11.93	<0.001	99.3	<0.001
		1–2 m	5	108	3.79	3.20	4.39	1.13	6.46	<0.001	88.6	<0.001
		3–6m[a]	1	25	0.38	0.18	0.58	NA	NA	<0.001		
	Type of surgery	Non-regenerative	3	53	3.92	−0.41	8.25	−53.04	59.89	0.076	99.5	<0.001
		Regenerative	7	126	3.81	3.38	4.23	2.39	5.22	<0.001	85.4	<0.001
		Non-regenerative (during ortho)[a]	1	25	0.44	0.26	0.61	NA	NA	<0.001		
	Type of ortho movement	Intrusion	7	116	3.35	1.85	4.86	−2.16	8.87	<0.001	99.1	<0.001
		Extrusion	4	98	3.80	3.29	4.31	1.44	6.17	<0.001	89.1	<0.001
	Type of anchorage	Conventional	5	80	4.57	3.49	5.64	0.43	88.71	<0.001	94.0	<0.001
		NR	1	10	3.70	2.60	4.79	NA	NA	<0.001		
		Mixed	5	124	2.45	0.85	4.05	−3.90	8.80	0.003	99.6	<0.001
PPD changes (mm)	Overall		12	302	3.47	2.63	4.30	0.18	6.75	<0.001	98.6	<0.001
	Interval periodontal & orthodontic therapy	≤2 weeks	7	159	3.66	2.98	4.33	1.38	5.94	<0.001	93.7	<0.001
		1–2 m	4	84	3.90	3.29	4.51	1.23	6.57	<0.001	83.7	<0.001
		3–6m[a]	1	59	1.18	1.04	1.32	NA	NA	<0.001		
	Type of surgery	Non-regenerative	3	102	3.83	2.74	4.91	−9.79	17.45	<0.001	95.3	<0.001
		Regenerative	8	111	3.76	3.28	4.23	2.22	5.30	<0.001	84.9	<0.001
		NR	1	59	1.18	1.04	1.32	NA	NA	<0.001		
	Type of ortho movement	Intrusion	8	204	3.42	2.39	4.45	−0.37	7.20	<0.001	98.9	<0.001
		Extrusion	4	98	3.82	3.10	4.55	0.75	6.90	<0.001	86.0	<0.001
	Type of anchorage	Conventional	7	159	3.66	2.98	4.33	1.38	5.94	<0.001	93.7	<0.001
		NR	2	69	2.38	−0.09	4.84	NA	NA	0.059	95.0	<0.001
		Mixed	3	10	3.94	3.24	4.65	−4.70	12.59	<0.001	89.1	<0.001

(Continues)

TABLE 7 (Continued)

Outcomes	Subgroups	Categories	*n* study	*n* patients	ME	95% CI		95% PI		*p*	I^2	*p*
						Lower	Upper	Lower	Upper			
RBL changes (mm)	Overall		6	112	2.76	0.77	4.74	−4.63	10.14	<0.001	100.0	<0.001
	Interval periodontal & orthodontic therapy	<2 weeks	3	38	1.36	0.01	2.72	−15.57	18.29	0.049	96.3	<0.001
		1–2 m	3	74	4.00	3.23	4.76	−5.85	13.85	<0.001	99.2	<0.001
	Type of surgery	Non-regenerative	1	10	1.35	0.89	1.82	NA	NA	<0.001		
		Regenerative	4	77	3.88	3.17	4.58	0.62	7.14	<0.001	98.8	<0.001
		Non-regenerative (during ortho)	1	25	0.02	−0.02	0.06	NA	NA	0.317		
	Type of ortho movement	Intrusion	3	38	1.361	0.00	2.72	−15.57	18.29	0.049	96.3	<0.001
		Extrusion	3	74	4.00	3.23	4.76	−5.85	13.85	<0.001	99.2	<0.001
	Type of anchorage	Conventional	2	13	2.15	0.38	3.92	NA	NA	0.017	85.0	0.01
		Mixed	4	99	3.01	0.57	5.44	−8.94	14.95	0.015	100.0	<0.001

Abbreviations: CAL, clinical attachment level; CI, confidence interval; I2, heterogeneity; ME, mean effect; mm, millimetres; m, months; NR, not reported; PPD, probing pocket depth; RBL, radiographic bone loss; REC, recession.

bias ($p = 0.041$ and $p = 0.013$, respectively). Visual inspection of the funnel plot showed 18 comparisons coming from 14 studies, in which an asymmetric pattern can be observed, suggesting that only studies with small sample size and positive results were published.

Post hoc sensitivity analysis was performed excluding studies one by one from the global estimation. No significant difference in the global estimator was found after excluding each study. However, after an overall visual analysis of the distribution of the specific estimators of each publication, it could be clearly observed that the results from (Zasčiurinskienė et al., 2018, 2019a, 2019b) did not follow the same pattern, which might be attributed to methodological differences (general vs local location, resective vs regenerative surgeries). Therefore, CAL change within the established subgroup was calculated with (n = 11; ME = 3.523 mm; 95% CI [2.353; 4.693]; $p < 0.001$) and without this study (n = 9; ME = 4.209 mm; 95% CI [3.614; 4.803]; $p < 0.001$).

The quality of the evidence was assessed using the GRADE approach. According to the GRADE guidelines, case series and case reports that investigate only patients exposed to an intervention provide low-quality evidence. The lack of a control group downgrades from low to very low-quality evidence. Appendix S15 shows that considering the periodontal variables reported in the included studies, the quality of the evidence was very low for all of them.

4 | DISCUSSION

This systematic review has demonstrated that (1) existing evidence on the orthodontic treatment of patients with previous severe periodontitis is very limited and of poor quality; being mostly pre–post-case series (with no control group) with high risk of bias; (2) in patients without periodontitis or with stable treated periodontitis (baseline measurements given after periodontal therapy), minimal changes in CAL, PPD or BOP were reported during orthodontic therapy ($p > 0.05$); (3) in periodontitis patients with baseline measurements reported before periodontal therapy, a significant CAL gain and PPD reduction was observed; (4) in this latter group of patients, the highest CAL gain was observed for conventional anchorage; (5) orthodontic outcomes were scarcely reported and objective assessment of the results on orthodontic therapy were missing.

4.1 | Effects of orthodontic therapy on periodontal outcomes (PICO #1)

Although there are previous narrative reviews explaining the effects of orthodontic therapy on periodontitis patients (Geisinger et al., 2014; Gyawali & Bhattarai, 2017; Ong & Wang, 2002), recent systematic reviews have mainly dealt with periodontally healthy participants, including only adolescents or specifically excluding advanced periodontitis cases (stage IV periodontitis) (Bollen et al., 2008; Cerroni et al., 2018; Gkantidis et al., 2010; Jiang et al., 2018;

Lu et al., 2018; Papageorgiou & Eliades, 2019; Papageorgiou et al., 2018; Rossini et al., 2015; Verrusio et al., 2018). Therefore, to our knowledge, this is the first systematic review dealing with periodontal outcomes in adult periodontitis patients, limiting a direct comparison with other studies.

Our results from non-periodontitis and periodontitis patients where periodontal outcomes were measured after periodontal therapy (stable treated periodontitis cases) (Chapple et al., 2018), are in line with the results published in the above mentioned systematic reviews; demonstrating that orthodontic treatment in participants with gingival health had little to no clinically relevant effect on CAL or PPD changes. It is important to note that some of the studies included in those systematic reviews were not included in this manuscript due to differences in the inclusion criteria, mainly mean age ≥18 years old and follow-up longer than 6 months from baseline.

Studies with periodontitis patients where periodontal outcomes were reported before periodontal therapy, and therefore, representing untreated periodontitis cases (Chapple et al., 2018) showed a mean CAL gain (mm) (ME = 3.523; 95% CI [2.353; 4.693]; $p < 0.001$) and a PPD reduction (mm) (ME = 3.466; 95% CI [2.630; 4.303]; $p < 0.001$) after orthodontic treatment, which are markedly positive effects. These results could be compared with those coming from the periodontal literature (before and after periodontal therapy). As it can be observed, the obtained results are even better than those reported in a recent systematic review (Sanz-Sánchez et al., 2020), in which access flap surgery in all type of periodontal defects (including intrabony defects) was performed, obtaining a significant CAL gain (ME = 1.31 mm; 95% CI [0.90; 1.71]; $p < 0.001$) and PPD reduction (ME = 2.94 mm; 95% CI [2.76; 3.13]; $p < 0.001$). Other systematic reviews dealing with resective surgery in furcation areas (Dommisch et al., 2020) or regenerative therapy in intrabony defects (Nibali et al., 2019), reported mean differences or survival rates instead of ME; and therefore, data could not be compared. However, it has to be considered that many of the studies included in the MA where related to assessment of improvement in CAL related to a vertical bone defect.

Regarding the best moment to apply orthodontic forces in periodontitis patients, three main time points were found in the literature: less than 2 weeks, 1–2 months or more that 3 months after periodontal surgeries. The best results were observed when the active force was applied 2 months after the patients were periodontally controlled. The optimal timing of active orthodontics after regenerative therapy was not quantitatively analysed in this review, since studies reported data in different ways. In some of the included studies (Aimetti et al., 2020; Ghezzi et al., 2008) orthodontic treatment was postponed for 1 year to avoid interference with periodontal wound healing. However, other reports suggested that orthodontic therapy may be initiated much earlier (Attia et al., 2019; Cardaropoli et al., 2006; Ghezzi et al., 2008; Ogihara & Tarnow, 2015; Ogihara & Wang, 2010), suggesting that there might be a significant positive effect of additional orthodontic tooth movements after regenerative therapy compared to regenerative therapy alone. In a CCT with 15 patients, Attia et al. (2012) in which immediate orthodontic therapy was compared to a delayed approach, a more favourable regenerative outcome was observed when the active movement was performed immediately after the surgical therapy. There was even one RCT (Zasčiurinskienė et al., 2018, 2019a, 2019b) that included periodontitis patients treated during or before orthodontic therapy, and whose rationale was to compare the application of orthodontic forces before or after periodontal therapy. However, it is important to consider, that they reported CAL changes attributed to periodontal therapy from locations with CAL>=4mm were lower than those previously published (Sanz-Sánchez 2020). This might indicate a limited impact of the periodontal therapy in the periodontal outcomes, which would be in contrast with the recent clinical guidelines (Sanz et al., 2020), and therefore, caution should be taken when analysing them.

When considering the type of orthodontic appliances, in all of the included studies fixed appliances were used; and therefore, no comparisons could be made. However, there was one study (Karkhanechi et al., 2013) in which a comparison between fixed and removable appliances was performed in non-periodontitis patients. As they reported in the results, the treatment with fixed buccal orthodontic appliances was associated with a worsen periodontal condition when compared to treatment with removable aligners, which is in agreement with previous systematic reviews results (Jiang et al., 2018; Lu et al., 2018).

4.2 | Orthodontic outcomes in periodontitis patients with skeletal anchorage (PICO #2)

Regarding the efficacy of skeletal anchorage in the orthodontic results of periodontitis patients, very few studies reported separate data for patients with and without skeletal anchorage used during OTM. Many studies mentioned the use of implants or TADs as anchorage for some tooth movements, but results were mixed for both types of patients. Intrusion was the most commonly reported outcome, but no comparison could be made since the conventional group reported intrusion of incisors (Cardaropoli et al., 2004; Corrente et al., 2003) and the skeletal group reported intrusion of molars (Heravi et al., 2011b; S. J. Lee, Miyazawa, et al., 2013). Due to anatomical differences (one versus three roots), the comparison of these results could not be performed.

4.3 | Limitations

It is important to consider the limitations associated with the present study, which involved: (1) scarcity of the existing evidence and the broadness of the research question, as RCTs, CCTs, prospective or retrospective clinical cohort studies or case series studies with pre- and post-treatment measures with at least 6 months of total duration follow-up were included. These implied, that direct mean differences comparing periodontitis and non-periodontitis patients could not be done; (2) scarce information regarding orthodontic outcomes for the PICO #2 question, and

whose results were finally combined with those from PICO #1; (3) wide variability in terms of periodontitis definitions (from mainly localized defects, to more generalized cases), periodontal therapy (SRP, non-regenerative or regenerative surgeries), periodontal outcomes measurements (from localized teeth to full-mouth approaches) and time of baseline periodontal outcomes collection (before or after periodontal therapy); (4) in meta-analyses, each arm of an included RCT or CCT was considered as an independent study and combined with case series to determine mean effects before and after OTM; and (5) heterogeneous clinical and statistical responses among studies were seen for most outcomes in the analyses, which is to be expected due to the wide spectrum of baseline severity / appliances / clinical protocols.

Therefore, and based on the studies included in this review, we conclude that, in non-periodontitis and in stable treated periodontitis patients, OTM had no significant impact on periodontal outcomes. Several studies on untreated periodontitis patients, that provided a baseline before a combined periodontal and orthodontic therapy reported significant improvements in periodontal outcomes. Thus, it may be assumed that these improvements were mainly due to the periodontal treatment component and that the orthodontic tooth movement did not interfere with periodontal healing.

However, due to the small number of studies and poor design of many of them, conclusions drawn from this review should be taken with caution.

4.4 | Implications for research

Future cohort studies with low risk of bias comparing orthodontic therapy in periodontitis and non-periodontitis patients, and addressing orthodontic (results of treatment and type of anchorage) and periodontal outcomes in three time points (before any therapy, after periodontal therapy and after orthodontic therapy) are desired.

4.5 | Implications for clinical practice

- Existing evidence on the orthodontic treatment of patients with severe periodontitis is very limited and of poor quality.
- Orthodontic therapy can be safely performed in treated periodontitis patients
- However, the optimal treatment protocol regarding time interval between orthodontic and periodontal therapies is not clear.
- There seems to be no evidence of added benefits on periodontal parameters from any type of anchorage devices used during orthodontic therapy.

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CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest directly related to this article.

AUTHORS' CONTRIBUTIONS

Conchita Martin (CM), Beatriz Celis (BC), Nagore Ambrosio (NA), Juan Bollain (JB), Georgios Antonoglou (GA), Elena Figuero (EF) CM and EF developed the study protocol, ran searches and extracted hits. BC, NA, JB and GA did study selection and data extraction. GA and CM did risk of bias assessment. EF did statistical analysis. BC, NA and JB wrote the Results tables. GA wrote the SoF tables. All authors assisted in the interpretation of results. EF and CM wrote the first manuscript draft. All authors revised the manuscript draft and approved the final version. CM is the corresponding author. CM and EF are guarantors of the present review and responsible for any updates.

DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions.

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REFERENCES

Aimetti, M., Garbo, D., Ercoli, E., Grigorie, M. M., Citterio, F., & Romano, F. (2020). Long-term prognosis of severely compromised teeth following combined periodontal and orthodontic treatment: a retrospective study. *International Journal of Periodontics & Restorative Dentistry*, *40*(1), 95–102. https://doi.org/10.11607/prd.4523.

Arn, M. L., Dritsas, K., Pandis, N., & Kloukos, D. (2020). The effects of fixed orthodontic retainers on periodontal health: A systematic review. *American Journal of Orthodontics and Dentofacial Orthopedics*, *157*(2), 156–164.e17. https://doi.org/10.1016/j.ajodo.2019.10.010.

Attia, M. S., Hazzaa, H. H., Al-Aziz, F. A., & Elewa, G. M. (2019). Evaluation of Adjunctive Use of Low-Level Diode Laser Biostimulation with Combined Orthodontic Regenerative Therapy. *Journal of the International Academy of Periodontology*, *21*(2), 63–73.

Attia, M. S., Shoreibah, E. A., Ibrahim, S. A., & Nassar, H. A. (2012). Regenerative therapy of osseous defects combined with orthodontic tooth movement. *Journal of the International Academy of Periodontology*, *14*(1), 17–25.

Bayani, S., Heravi, F., Radvar, M., Anbiaee, N., & Madani, A. S. (2015). Periodontal changes following molar intrusion with miniscrews. *Dental Research Journal*, *12*(4), 379–385. https://doi.org/10.4103/1735-3327.161462.

Beller, E. M., Glasziou, P. P., Altman, D. G., Hopewell, S., Bastian, H., Chalmers, I., & Group, P. f. A (2013). PRISMA for Abstracts: reporting systematic reviews in journal and conference abstracts. *PLoS Medicine*, *10*(4), e1001419. https://doi.org/10.1371/journal.pmed.1001419.

Bollen, A.-M., Cunha-Cruz, J., Bakko, D. W., Huang, G. J., & Hujoel, P. P. (2008). The effects of orthodontic therapy on periodontal health - A systematic review of controlled evidence. *Journal of the American Dental Association*, *139*(4), 413–422. https://doi.org/10.14219/jada.archive.2008.0184.

Brook, P. H., & Shaw, W. C. (1989). The development of an index of orthodontic treatment priority. *European Journal of Orthodontics*, *11*(3), 309–320. https://doi.org/10.1093/oxfordjournals.ejo.a035999.

Brown, I. S. (1973). The effect of orthodontic therapy on certain types of periodontal defects. *I. Clinical Findings. Journal of Periodontology*, *44*(12), 742–756. https://doi.org/10.1902/jop.1973.44.12.742.

Cangialosi, T. J., Riolo, M. L., Owens, S. E., Dykhouse, V. J., Moffitt, A. H., Grubb, J. E., Greco, P. M., English, J. D., & James, R. D. (2004). The ABO discrepancy index: a measure of case complexity. *American Journal of Orthodontics and Dentofacial Orthopedics*, *125*(3), 270–278. https://doi.org/10.1016/j.ajodo.2004.01.005.

Cao, T., Xu, L. X., Shi, J. J., & Zhou, Y. (2015). Combined orthodontic-periodontal treatment in periodontal patients with anteriorly displaced incisors. *American Journal of Orthodontics and Dentofacial Orthopedics*, *148*(5), 805–813. https://doi.org/10.1016/j.ajodo.2015.05.026.

Cardaropoli, D., Re, S., Corrente, G., & Abundo, R. (2004). Reconstruction of the maxillary midline papilla following a combined orthodontic-periodontic treatment in adult periodontal patients. *Journal of Clinical Periodontology*, *31*(2), 79–84. https://doi.org/10.1111/j.0303-6979.2004.00451.x.

Cardaropoli, D., Re, S., Manuzzi, W., Gaveglio, L., & Cardaropoli, G. (2006). Bio-oss collagen and orthodontic movement for the treatment of infrabony defects in the esthetic zone. *International Journal of Periodontics & Restorative Dentistry*, *26*(6), 553–559.

Carrasco-Labra, A., Brignardello-Petersen, R., Santesso, N., Neumann, I., Mustafa, R. A., Mbuagbaw, L., Etxeandia Ikobaltzeta, I., De Stio, C., McCullagh, L. J., Alonso-Coello, P., Meerpohl, J. J., Vandvik, P. O., Brozek, J. L., Akl, E. A., Bossuyt, P., Churchill, R., Glenton, C., Rosenbaum, S., Tugwell, P., … Schünemann, H. J. (2016). Improving GRADE evidence tables part 1: a randomized trial shows improved understanding of content in summary of findings tables with a new format. *Journal of Clinical Epidemiology*, *74*, 7–18. https://doi.org/10.1016/j.jclinepi.2015.12.007.

Carvalho, C. V., Saraiva, L., Bauer, F. P. F., Kimura, R. Y., Souto, M. L. S., Bernardo, C. C., Pannuti, C. M., Romito, G. A., & Pustiglioni, F. E. (2018). Orthodontic treatment in patients with aggressive periodontitis. *American Journal of Orthodontics and Dentofacial Orthopedics*, *153*(4), 550–557. https://doi.org/10.1016/j.ajodo.2017.08.018.

Casko, J. S., Vaden, J. L., Kokich, V. G., Damone, J., James, R. D., Cangialosi, T. J., Riolo, M. L., Owens, S. E., & Bills, E. D. (1998). Objective grading system for dental casts and panoramic radiographs. American Board of Orthodontics. *Americal Journal of Orthodontics and Dentofacial Orthopedics*, *114*(5), 589–599. https://doi.org/10.1016/s0889-5406(98)70179-9.

Cerroni, S., Pasquantonio, G., Condò, R., & Cerroni, L. (2018). Orthodontic Fixed Appliance and Periodontal Status: An Updated Systematic Review. *Open Dental Journal*, *12*, 614–622. https://doi.org/10.2174/1745017901814010614.

Chapple, I. L. C., Mealey, B. L., Van Dyke, T. E., Bartold, P. M., Dommisch, H., Eickholz, P., Geisinger, M. L., Genco, R. J., Glogauer, M., Goldstein, M., Griffin, T. J., Holmstrup, P., Johnson, G. K., Kapila, Y., Lang, N. P., Meyle, J., Murakami, S., Plemons, J., Romito, G. A., … Yoshie, H. (2018). Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of Clinical Periodontology*, *45*(Suppl 20), S68–S77. https://doi.org/10.1111/jcpe.12940.

Corrente, G., Abundo, R., Re, S., Cardaropoli, D., & Cardaropoli, G. (2003). Orthodontic movement into infrabony defects in patients with advanced periodontal disease: A clinical and radiological study. *Journal of Periodontology*, *74*(8), 1104–1109. https://doi.org/10.1902/jop.2003.74.8.1104.

Cumpston, M., Li, T., Page, M. J., Chandler, J., Welch, V. A., Higgins, J. P., & Thomas, J. (2019). Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Database of Systematic Reviews*, *10*, ED000142. https://doi.org/10.1002/14651858.ED000142

Dommisch, H., Walter, C., Dannewitz, B., & Eickholz, P. (2020). Resective surgery for the treatment of furcation involvement - a systematic review. *Journal of Clinical Periodontology*, https://doi.org/10.1111/jcpe.13241.

Eliasson, L. A., Hugoson, A., Kurol, J., & Siwe, H. (1982). The effects of orthodontic treatment on periodontal tissues in patients with reduced periodontal support. *European Journal of Orthodontics*, *4*(1), 1–9. https://doi.org/10.1093/ejo/4.1.1.

Geisinger, M. L., Abou-Arraj, R. V., Souccar, N. M., Holmes, C. M., & Geurs, N. C. (2014). Decision making in the treatment of patients with malocclusion and chronic periodontitis: Scientific evidence and clinical experience. *Seminars in Orthodontics*, *20*(3), 170–176. https://doi.org/10.1053/j.sodo.2014.06.006.

Ghezzi, C., Masiero, S., Silvesth, M., Zanotti, G., & Rasperini, G. (2008). Orthodontic treatment of periodontally involved teeth after tissue regeneration. *International Journal of Periodontics & Restorative Dentistry*, *28*(6), 559–567.

Gkantidis, N., Christou, P., & Topouzelis, N. (2010). The orthodontic-periodontic interrelationship in integrated treatment challenges: a systematic review. *Journal of Oral Rehabilitation*, *37*(5), 377–390. https://doi.org/10.1111/j.1365-2842.2010.02068.x.

Gomes, S. C., Varela, C. C., da Veiga, S. L., Rosingm, C. K., & Oppermannm, R. V. (2007). Periodontal conditions in subjects following orthodontic therapy. A preliminary study. *European Journal of Orthodontics*, *29*(5), 477–481. https://doi.org/10.1093/ejo/cjm050.

Guyatt, G., Oxman, A. D., Akl, E. A., Kunz, R., Vist, G., Brozek, J., Norris, S., Falck-Ytter, Y., Glasziou, P., & deBeer, H. (2011). GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *Journal of Clinical Epidemiology*, *64*(4), 383–394. https://doi.org/10.1016/j.jclinepi.2010.04.026.

Gyawali, R., & Bhattarai, B. (2017). Orthodontic Management in Aggressive Periodontitis. *International Scholary Research Notices*, *2017*, 8098154. https://doi.org/10.1155/2017/8098154.

Harris, E. F., & Baker, W. C. (1990). Loss of root length and crestal bone height before and during treatment in adolescent and adult orthodontic patients. *American Journal of Orthodontics and Dentofacial Orthopedics*, *98*(5), 463–469. https://doi.org/10.1016/s0889-5406(05)81656-7.

Heravi, F., Bayani, S., Madani, A. S., Radvar, M., & Anbiaee, N. (2011a). Intrusion of supra-erupted molars using miniscrews: clinical success and root resorption. *American Journal of Orthodontics and Dentofacial Orthopedics*, *139*(4 Suppl), S170–175. https://doi.org/10.1016/j.ajodo.2009.06.032.

Heravi, F., Bayani, S., Madani, A. S., Radvar, M., & Anbiaee, N. (2011b). Intrusion of supra-erupted molars using miniscrews: clinical success and root resorption. *American Journal of Orthodontics and Dentofacial Orthopedics*, *139*(4 Suppl), S170–175. https://doi.org/10.1016/j.ajodo.2009.06.032.

IntHout, J., Ioannidis, J. P., Rovers, M. M., & Goeman, J. J. (2016). Plea for routinely presenting prediction intervals in meta-analysis. *British Medical Journal Open*, *6*(7), e010247. https://doi.org/10.1136/bmjopen-2015-010247.

Jiang, Q., Li, J., Mei, L., Du, J., Levrini, L., Abbate, G. M., & Li, H. (2018). Periodontal health during orthodontic treatment with clear aligners and fixed appliances: A meta-analysis. *Journal of the American Dental*

Association, *149*(8), 712–720.e712. https://doi.org/10.1016/j.adaj.2018.04.010.

Kanomi, R. (1997). Mini-implant for orthodontic anchorage. *Jounal of Clinical Orthodontics*, *31*(11), 763–767.

Karkhanechi, M., Chow, D., Sipkin, J., Sherman, D., Boylan, R. J., Norman, R. G., Craig, R. G., & Cisneros, G. J. (2013). Periodontal status of adult patients treated with fixed buccal appliances and removable aligners over one year of active orthodontic therapy. *Angle Orthodontist*, *83*(1), 146–151. https://doi.org/10.2319/031212-217.1.

Lee, J., Miyazawa, K., Tabuchi, M., Kawaguchi, M., Shibata, M., & Goto, S. (2013). Midpalatal miniscrews and high-pull headgear for anteroposterior and vertical anchorage control: Cephalometric comparisons of treatment changes. *American Journal of Orthodontics and Dentofacial Orthopedics*, *144*(2), 238–250. https://doi.org/10.1016/j.ajodo.2013.03.020.

Lee, S. J., Jang, S. Y., Chun, Y. S., & Lim, W. H. (2013). Three-dimensional analysis of tooth movement after intrusion of a supraerupted molar using a mini-implant with partial-fixed orthodontic appliances. *Angle Orthodontist*, *83*(2), 274–279. https://doi.org/10.2319/060912-480.1.

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P. A., Clarke, M., Devereaux, P. J., Kleijnen, J., & Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Journal of Clinical Epidemiology*, *62*(10), e1–34. https://doi.org/10.1016/j.jclinepi.2009.06.006.

Liu, H., Mou, Y. D., Yu, X. G., Peng, F. Y., Li, Q. H., & Deng, F. H. (2016). Stability and safety of mini-implant anchorage in orthodontic treatment. *Chinese Journal of Tissue Engineering Research*, *20*(8), 1159–1164. https://doi.org/10.3969/j.Issn.2095-4344.2016.08.014.

Lu, H., Tang, H., Zhou, T., & Kang, N. (2018). Assessment of the periodontal health status in patients undergoing orthodontic treatment with fixed appliances and Invisalign system: A meta-analysis. *Medicine (Baltimore)*, *97*(13), e0248. https://doi.org/10.1097/md.0000000000010248.

Melsen, B., Agerbaek, N., & Markenstam, G. (1989). Intrusion of incisors in adult patients with marginal bone loss. *American Journal of Orthodontics and Dentofacial Orthopedics*, *96*(3), 232–241. https://doi.org/10.1016/0889-5406(89)90460-5.

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Journal of Clinical Epidemiology*, *62*(10), 1006–1012. https://doi.org/10.1016/j.jclinepi.2009.06.005.

Nanda, R. S., & Kierl, M. J. (1992). Prediction of cooperation in orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics*, *102*(1), 15–21. https://doi.org/10.1016/0889-5406(92)70010-8.

NHLBI, N. H., Lung, and Blood Institute (2014). *Study quality assessment tools. Quality assessment tool for before-after (Pre-Post) studies with no control group*. Retrieved from https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools.

Nibali, L., Koidou, V. P., Nieri, M., Barbato, L., Pagliaro, U., & Cairo, F. (2019). Regenerative surgery versus access flap for the treatment of intra-bony periodontal defects: A systematic review and meta-analysis. *Journal of Clinical Periodontology*, *47*(S22), 320–351. https://doi.org/10.1111/jcpe.13237.

Ödman, J., Lekholm, U., Jemt, T., & Thilander, B. (1994). Osseointegrated implants as orthodontic anchorage in the treatment of partially edentulous adult patients. *European Journal of Orthodontics*, *16*(3), 187–201. https://doi.org/10.1093/ejo/16.3.187.

Ogihara, S., & Tarnow, D. P. (2015). Efficacy of forced eruption/enamel matrix derivative with freeze-dried bone allograft or with demineralized freeze-dried bone allograft in infrabony defects: A randomized trial. *Quintessence International*, *46*(6), 481–490. https://doi.org/10.3290/j.qi.a33936.

Ogihara, S., & Wang, H.-L. (2010). Periodontal regeneration with or without limited orthodontics for the treatment of 2- or 3-wall infrabony defects. *Journal of Periodontology*, *81*(12), 1734–1742. https://doi.org/10.1902/jop.2010.100127.

Ong, M. M. A., & Wang, H. L. (2002). Periodontic and orthodontic treatment in adults. *American Journal of Orthodontics and Dentofacial Orthopedics*, *122*(4), 420–428. https://doi.org/10.1067/mod.2002.126597.

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T., Mulrow, C. D., Shamseer, L., & Moher, D. (2020). Mapping of reporting guidance for systematic reviews and meta-analyses generated a comprehensive item bank for future reporting guidelines. *Journal of Clinical Epidemiology*, *118*, 60–68. https://doi.org/10.1016/j.jclinepi.2019.11.010.

Papadopoulos, M. A., Papageorgiou, S. N., & Zogakis, I. P. (2011). Clinical effectiveness of orthodontic miniscrew implants: a meta-analysis. *Journal Dental Research*, *90*(8), 969–976. https://doi.org/10.1177/0022034511409236.

Papageorgiou, S. N., & Eliades, T. (2019). Clinical Evidence on the effect of orthodontic treatment on the periodontal tissues. In T. Eliades, & C. Katsaros (Eds.), *The ortho-perio patient: clinical evidence & therapeutic guidelines* (pp. 161–173). Quintessence.

Papageorgiou, S. N., Papadelli, A. A., & Eliades, T. (2018). Effect of orthodontic treatment on periodontal clinical attachment: a systematic review and meta-analysis. *European Journal of Orthodontics*, *40*(2), 176–184. https://doi.org/10.1093/ejo/cjx052.

Papapanou, P. N., Sanz, M., Buduneli, N., Dietrich, T., Feres, M., Fine, D. H., Flemmig, T. F., Garcia, R., Giannobile, W. V., Graziani, F., Greenwell, H., Herrera, D., Kao, R. T., Kebschull, M., Kinane, D. F., Kirkwood, K. L., Kocher, T., Kornman, K. S., Kumar, P. S., … Tonetti, M. S. (2018). Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal Clinical of Periodontology*, *45*(Suppl 20), S162–s170. https://doi.org/10.1111/jcpe.12946.

Paraskevas, S., Huizinga, J. D., & Loos, B. G. (2008). A systematic review and meta-analyses on C-reactive protein in relation to periodontitis. *Journal of Clinical Periodontology*, *35*(4), 277–290. https://doi.org/10.1111/j.1600-051X.2007.01173.x.

Re, S., Cardaropoli, D., Abundo, R., & Corrente, G. (2004). Reduction of gingival recession following orthodontic intrusion in periodontally compromised patients. *Orthodontics & Craniofacial Research*, *7*(1), 35–39. https://doi.org/10.1111/j.1601-6343.2004.00277.x.

Re, S., Corrente, G., Abundo, R., & Cardaropoli, D. (2000). Orthodontic treatment in periodontally compromised patients: 12-year report. *International Journal of Periodontics & Restorative Dentistry*, *20*(1), 31–39.

Richmond, S., Shaw, W. C., O'Brien, K. D., Buchanan, I. B., Jones, R., Stephens, C. D., Roberts, C. T., & Andrews, M. (1992). The development of the PAR Index (Peer Assessment Rating): reliability and validity. *European Journal of Orthodontics*, *14*(2), 125–139. https://doi.org/10.1093/ejo/14.2.125.

Rossini, G., Parrini, S., Castroflorio, T., Deregibus, A., & Debernardi, C. L. (2015). Periodontal health during clear aligners treatment: a systematic review. *European Journal of Orthodontics*, *37*(5), 539–543. https://doi.org/10.1093/ejo/cju083.

Sadiq, S. M. A., & Badea, R. A. (2012). A Longitudinal investigation of the Periodontal changes in adult and adolescent orthodontic patients using bands or bonds on molars. Paper presented at the Mustansiria Dental Journal

Sanz, M., Herrera, D., Kebschull, M., Chapple, I., Jepsen, S., Berglundh, T., Sculean, A., Tonetti, M. S., Merete Aass, A., Aimetti, M., Kuru, B. E., Belibasakis, G., Blanco, J., Bol-van den Hil, E., Bostanci, N., Bozic, D., Bouchard, P., Buduneli, N., Cairo, F., … Wennström, J. (2020). Treatment of stage I-III periodontitis -The EFP S3 level clinical practice guideline. *Journal of Clinical Periodontology*, *47*(S22), 4–60. https://doi.org/10.1111/jcpe.13290.

Sanz-Sánchez, I., Carrillo de Albornoz, A., Figuero, E., Schwarz, F., Jung, R., Sanz, M., & Thoma, D. (2018). Effects of lateral bone augmentation

procedures on peri-implant health or disease: A systematic review and meta-analysis. *Clinical Oral Implants Research*, *29*(Suppl 15), 18–31. https://doi.org/10.1111/clr.13126.

Sanz-Sánchez, I., Montero, E., Citterio, F., Romano, F., Molina, A., & Aimetti, M. (2020). Efficacy of access flap procedures compared to subgingival debridement in the treatment of periodontitis. A systematic review and meta-analysis. *Journal of Clinical Periodontology*, *47*(S22), 282–302. https://doi.org/10.1111/jcpe.13259.

Sanz-Sánchez, I., Ortiz-Vigón, A., Sanz-Martín, I., Figuero, E., & Sanz, M. (2015). Effectiveness of lateral bone augmentation on the alveolar crest dimension: a systematic review and meta-analysis. *Journal Dental Research*, *94*(9 Suppl), 128s–142s. https://doi.org/10.1177/0022034515594780.

Schünemann, H. J., Cuello, C., Akl, E. A., Mustafa, R. A., Meerpohl, J. J., Thayer, K., Morgan, R. L., Gartlehner, G., Kunz, R., Katikireddi, S. V., Sterne, J., Higgins, J. P. T., & Guyatt, G. (2019). GRADE guidelines: 18. How ROBINS-I and other tools to assess risk of bias in nonrandomized studies should be used to rate the certainty of a body of evidence. *Journal of Clinical Epidemiology*, *111*, 105–114. https://doi.org/10.1016/j.jclinepi.2018.01.012.

Sterne, J. A. C., Hernán, M. A., Reeves, B. C., Savović, J., Berkman, N. D., Viswanathan, M., Henry, D., Altman, D. G., Ansari, M. T., Boutron, I., Carpenter, J. R., Chan, A.-W., Churchill, R., Deeks, J. J., Hróbjartsson, A., Kirkham, J., Jüni, P., Loke, Y. K., Pigott, T. D., … Higgins, J. P. T. (2016). ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *British Medical Journal*, *355*, i4919. https://doi.org/10.1136/bmj.i4919.

Sterne, J. A. C., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., Cates, C. J., Cheng, H.-Y., Corbett, M. S., Eldridge, S. M., Emberson, J. R., Hernán, M. A., Hopewell, S., Hróbjartsson, A., Junqueira, D. R., Jüni, P., Kirkham, J. J., Lasserson, T., Li, T., … Higgins, J. P. T. (2019). RoB 2: a revised tool for assessing risk of bias in randomised trials. *British Medical Journal*, *366*, l4898. https://doi.org/10.1136/bmj.l4898.

Sugawara, J., Daimaruya, T., Umemori, M., Nagasaka, H., Takahashi, I., Kawamura, H., & Mitani, H. (2004). Distal movement of mandibular molars in adult patients with the skeletal anchorage system. *American Journal of Orthodontics and Dentofacial Orthopedics*, *125*(2), 130–138. https://doi.org/10.1016/j.ajodo.2003.02.003.

Tonetti, M. S., & Sanz, M. (2019). Implementation of the new classification of periodontal diseases: Decision-making algorithms for clinical practice and education. *Journal Clinical of Periodontology*, *46*(4), 398–405. https://doi.org/10.1111/jcpe.13104.

Trombelli, L., Franceschetti, G., & Farina, R. (2015). Effect of professional mechanical plaque removal performed on a long-term, routine basis in the secondary prevention of periodontitis: a systematic review. *Journal Clinical of Periodontology*, *42*(Suppl 16), S221–236. https://doi.org/10.1111/jcpe.12339.

van Gastel, J., Quirynen, M., Teughels, W., Coucke, W., & Carels, C. (2011). Longitudinal changes in microbiology and clinical periodontal parameters after removal of fixed orthodontic appliances. *European Journal of Orthodontics*, *33*(1), 15–21. https://doi.org/10.1093/ejo/cjq032.

Verrusio, C., Iorio-Siciliano, V., Blasi, A., Leuci, S., Adamo, D., & Nicolò, M. (2018). The effect of orthodontic treatment on periodontal tissue inflammation: A systematic review. *Quintessence International*, *49*(1), 69–77. https://doi.org/10.3290/j.qi.a39225.

Wells, G. A., Shea, B., O'connell, D., Peterson, J., Welch, V., Losos, M., & Tugwell, P. (2015). *The Newcastle-Ottawa Scale (NOS) for Assessing the Quality if Nonrandomized Studies in Meta-Analyses*. Available online: http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm. (Accessed 1 May 2021)

Wennström, J. L., Stokland, B. L., Nyman, S., & Thilander, B. (1993). Periodontal tissue response to orthodontic movement of teeth with infrabony pockets. *American Journal of Orthodontics and Dentofacial Orthopedics*, *103*(4), 313–319. https://doi.org/10.1016/0889-5406(93)70011-C.

Zasčiurinskienė, E., Basevičienė, N., Lindsten, R., Slotte, C., Jansson, H., & Bjerklin, K. (2018). Orthodontic treatment simultaneous to or after periodontal cause-related treatment in periodontitis susceptible patients. Part I: Clinical outcome. A randomized clinical trial. *Journal of Clinical Periodontology*, *45*(2), 213–224. https://doi.org/10.1111/jcpe.12835.

Zasčiurinskienė, E., Lund, H., Lindsten, R., Jansson, H., & Bjerklin, K. (2019a). Outcome of orthodontic treatment in subjects with periodontal disease. Part III: a CBCT study of external apical root resorption. *European Journal of Orthodontics*, *41*(6), 575–582. https://doi.org/10.1093/ejo/cjz040.

Zasčiurinskienė, E., Lund, H., Lindsten, R., Jansson, H., & Bjerklin, K. (2019b). Outcome of periodontal-orthodontic treatment in subjects with periodontal disease. Part II: a CBCT study of alveolar bone level changes. *European Journal of Orthodontics*, *41*(6), 565–574. https://doi.org/10.1093/ejo/cjz039.

Zhang, J., Zhang, A. M., Zhang, Z. M., Jia, J. L., Sui, X. X., Yu, L. R., & Liu, H. T. (2017). Efficacy of combined orthodontic-periodontic treatment for patients with periodontitis and its effect on inflammatory cytokines: A comparative study. *Americal Journal of Orthodontics and Dentofacial Orthopedics*, *152*(4), 494–500. https://doi.org/10.1016/j.ajodo.2017.01.028.

Zoizner, R., Arbel, Y., Yavnai, N., Becker, T., & Birnboim-Blau, G. (2018). Effect of orthodontic treatment and comorbidity risk factors on interdental alveolar crest level: A radiographic evaluation. *American Journal of Orthodontics and Dentofacial Orthopedics*, *154*(3), 375–381. https://doi.org/10.1016/j.ajodo.2017.12.012.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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