## Seeking and reporting of adverse effects in orthodontic research

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Pauline A.J. Steegmans

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Pauline Antoinette Josephine Steegmans

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**Paranymphs**

Michiel Steegmans

Floor Tielbeke

**Dedication**

This dissertation is affectionately dedicated to my beloved father (in memoriam), mother and brother.

## Highlights of this dissertation

**What is new?**

**Key findings**

This dissertation summarized the results of 7 publications on adverse effects of orthodontic interventions. Key findings are:

- A new framework was developed to categorize and define adverse effects of orthodontic interventions.
- Relapse and stability issues (19% (36/195)) and undesired treatment results (22% (43/195)) were the predominant adverse effects sought and reported in systematic reviews of orthodontic interventions, but many adverse effects were underassessed and underreported.
- 36% (35/98) of systematic reviews of orthodontic interventions defined seeking of adverse effects of interventions as a research objective of the systematic review.
- 85% (83/98) of systematic reviews of orthodontic interventions reported findings related to adverse effects of interventions sought in the studies included in the review.
- 91% (89/98) of systematic reviews of orthodontic interventions considered, discussed (weighed) potential adverse effects of interventions somewhere in the manuscript.
- 77% (75/98) of systematic reviews of orthodontic interventions reported or considered (i.e., discussed, weighed) potential adverse effects of interventions in the abstracts.
- 41% (40/98) of systematic reviews of orthodontic interventions had spin on adverse effects in the abstracts of these reviews.
- Misleading reporting was the predominant type (90% (36/40)) of spin on adverse effects in the abstracts of systematic reviews of orthodontic interventions.

**What this adds to what was known?**

- This dissertation presented a new framework for categorizing and defining adverse effects of orthodontic interventions.
- This dissertation showed that most systematic reviews of orthodontic interventions assessed and reported adverse effects but these actions were not systematic, incomplete, and selective.
- This dissertation showed that reporting on adverse effects in abstracts of systematic reviews of orthodontic interventions was suboptimal with a high prevalence of spin.

**What is the implication and what should change now**

- This dissertation showed that what is assessed and reported on adverse effects in systematic reviews of orthodontic interventions was often incomplete and misleading, which could lead to inadequate clinical decision making.
- Focus on developing, assessing, and reporting of core adverse effects of orthodontic interventions (using our new framework) in primary studies and in systematic reviews.
- Besides conducting traditional systematic reviews of interventions, consider undertaking systematic reviews that focus exclusively on adverse effects.

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# CHAPTER 1

General introduction and objectives

**The central story**

Systematic reviews identify the current knowledge status on a particular health issue by synthesizing and appraising best evidence. When well conducted, these reviews save end-users considerable time, energy, and resources. However, when done poorly, these reviews can be misleading and even cause harm. This can be worrisome considering the high-quality status of systematic reviews in the evidence hierarchy [1] and the high and increasing number of such reviews published in the literature (Figure 1).

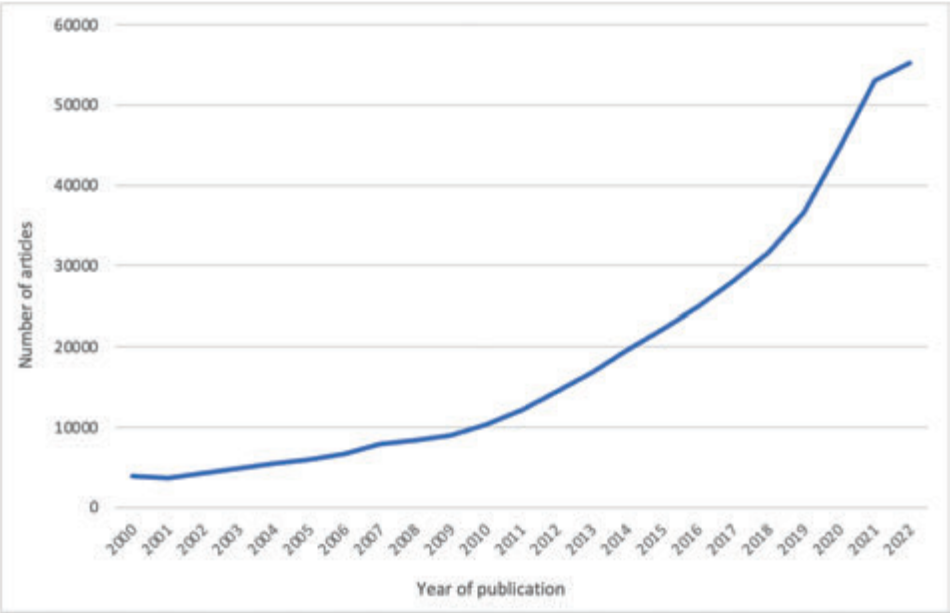


**Figure 1.** Line chart showing the exponential growth of systematic reviews of interventions in healthcare since 2000 in PubMed.
Search strategy in PubMed: (systematic review* AND (healthcare* OR health* OR intervention* OR therapy* OR treatment*))

The consequences of low-quality reviews could be even more damaging when the adverse effects of interventions are poorly assessed and reported. Therefore prior to implementing the findings of systematic reviews, clinicians need to critically appraise these studies and evaluate their credibility regarding the assessment and reporting of adverse effects of interventions. Cochrane states that “it is critical that outcomes used to assess adverse effects as well as outcomes used to assess beneficial effects are among those addressed by a review” [2]. It is also critical that when presenting findings on adverse effects that they are free of spin, i.e., a distorted presentation of study results [3]. This is particularly important in abstracts, because titles and abstracts are the most and often the only read sections of biomedical papers [4]. This dissertation assessed a broad spectrum of items on defining, seeking and reporting of adverse effects in systematic reviews of orthodontic interventions.

**Description of the condition**

Classifying and defining adverse effects of interventions is challenging [5,6]. For instance, harms, adverse events, side effects, complications, safety, and toxicity are closely related terms, but their definitions can vary between studies [7]. The definition of adverse effects depends on the context and type of intervention [6]. For example, in orthodontics, anchorage loss of first molars that are reinforced with implants can be considered an adverse effect. Instead, anchorage loss can also be a beneficial effect, e.g., in extraction cases where anchorage loss is desired to avoid over-retraction of maxillary incisors. In this dissertation, we adopted Cochrane's definition of an adverse effect: "An adverse event for which the causal relation between the intervention and the event is at least a reasonable possibility" [5].

Preoteasa et al. [8] categorized a variety of adverse effects of orthodontic interventions and presented them in a framework of subgroups (Table 1). Root resorption is an example of the dental subgroup of adverse effects linked to orthodontics and is illustrated in Figure 2. The framework by Preoteasa et al. [8] was used for defining and assessing adverse effects in the research studies of this dissertation. These assessments subsequently resulted in a new framework for defining adverse effects of orthodontic interventions, which is presented in additional file 2 of chapter 3, additional file 2 of chapter 5 and chapter 9.

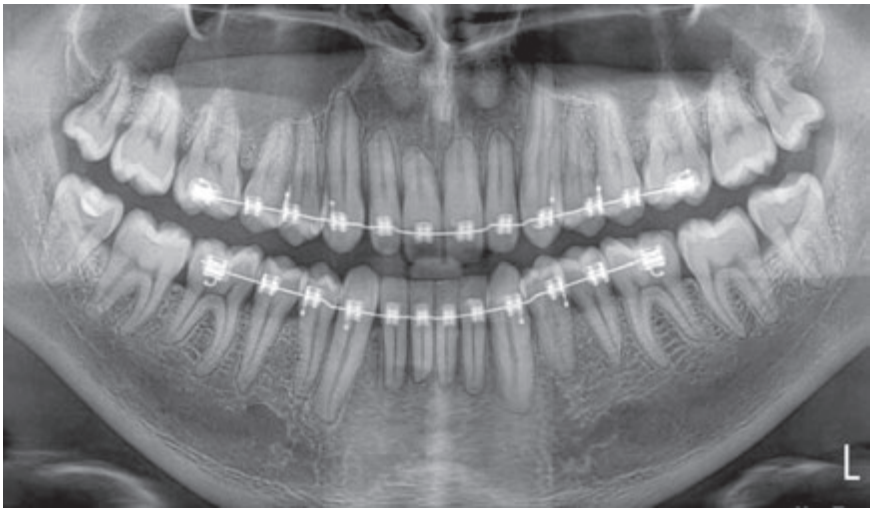


**Figure 2.** Root resorption is visible on a large number of maxillary and mandibular teeth [9]

**Table 1.** Adverse effects hypothetically linked to orthodontic interventions according to Preoteasa et al. [8]*

| Subgroup | Description |
|---|---|
| Local adverse effects | |
| Dental | • Crown: decalcifications, decays, tooth wear, enamel cracks and fractures; discolorations, deterioration of prosthetic crown (as fracturing a ceramic one during debonding)<br>• Root: root resorption, early closure of root apex, ankylosis<br>• Pulp: ischemia, pulpitis, necrosis |
| Periodontal | • Gingivitis, periodontitis, gingival recession or hypertrophy, alveolar bone loss, dehiscences, fenestrations, interdental fold, dark triangles |
| Temporomandibular joint | • Condylar resorption, temporomandibular dysfunction |
| Soft tissues of the oral and maxillofacial region | • Trauma (e.g., long archwires, headgear related), mucosal ulcerations or hyperplasia, chemical burns (e.g., etching related), thermal injuries (e.g., overheated burs), stomatitis, clumsy handling of dental instruments |
| Unsatisfactory treatment outcome | • Inadequate morpho-functional, esthetic or functional final result, relapse, failure to complete treatment due to treatment dropout |
| Systemic adverse effects | |
| Psychological | • Teasing, behavioral changes of patients and parents; discomfort associated with pain presence and esthetic look discontents during orthodontic appliance usage |
| Gastro-intestinal | • Accidental swallowing of small parts of the orthodontic device (tubes, brackets) |
| Allergies | • To nickel or latex |
| Cardiac | • Infective endocarditis |
| Chronic fatigue syndrome | |
| Cross infections | • From doctor to patient, patient to doctor, patient to patient |

*Permission to reproduce this table was obtained on 16 August 2018 from InTech's Publishing Ethics and Legal Affairs Department

**Description of the problems and what is published on the problems**

Three major methodological and reporting problems regarding adverse effects in systematic reviews can jeopardize the information published on these effects, which can subsequently affect clinical decision making.

1. *Poor seeking, reporting, and synthesizing of adverse effects of interventions in systematic reviews*

Epidemiological research has shown that seeking, reporting, and synthesizing of adverse effects of interventions was suboptimal in systematic reviews of interventions [10, 11, 12, 13, 14]. Poor methodological rigor in assessing adverse effects of interventions was also identified in Cochrane reviews [15]. The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) harms checklist was published in 2016 to improve the reporting of adverse effects in systematic reviews [7] but little evidence is available on the consequences of this reporting guideline on the quality of reporting of adverse effects in systematic reviews [16].

2. *Poor seeking, reporting, and synthesizing of adverse effects of interventions in primary studies*

The lack of rigor in seeking and reporting of adverse effects in the primary studies that feed systematic reviews is another major problem that affects the validity on what is reported on adverse effects in these reviews. Multiple epidemiological studies have identified these limitations in primary studies [17, 18, 19, 20, 21, 22]. For example, clinical trials on the evaluation of the same drugs showed that different adverse effects were assessed and reported [23, 24]. Further, a higher number and range of adverse effects were reported in unpublished versions of clinical trials compared to the final published versions of these trials [18]. To improve the reporting of adverse effects in randomized controlled trials (RCTs), an extension of the Consolidated Standards of Reporting Trials (CONSORT) was developed in 2004 [25]. Several studies have investigated the effect of this guideline on reporting adverse effects, but only slight improvements were found [17, 19, 20, 26].

3. *Misleading reporting, interpretation, and extrapolation (spin) of adverse effects in systematic reviews.*

Misleading presentation of study results regarding adverse effects is a major problem that can affect clinical decision making. Distorted presentation of study results is called 'spin' [3]. A wide variety of terms and definitions have been used for spin in the medical literature. For example; misrepresentation [27, 28], distorted presentation [29], inappropriate extrapolation [28], overinterpretation, and misreporting [30]. Spin has been divided into three subcategories: 'misleading reporting', 'misleading interpretation', and 'misleading extrapolation' of study results [31]. This dissertation will adopt the definitions described by Lazarus et al. [32] for these three categories of spin. Table 2 gives an overview of these definitions and key terminology used in this dissertation.

Spin in the abstracts of research studies can be particularly harmful because titles and abstracts are the most read and often also the only read sections of biomedical papers [4]. The presence of spin in abstracts can influence readers' interpretation [27], which could result in inadequate decisions on healthcare interventions. The Methodological Expectations of Cochrane Intervention Reviews (MECIR) state: "The abstract of the review should aim to reflect a balanced summary of the benefits and harms of the intervention" [40]. Epidemiological studies have examined the presence of spin in abstracts of randomized controlled trials and systematic reviews in different research fields [27, 29, 41, 42, 43, 44]. Such studies identified spin in more than 50% of abstracts of medical RCTs [29, 43, 45], and in more than 30% of abstracts of systematic reviews of proximal humerus fractures treatments [46]. Similar findings were reported in orthodontic RCTs [42] and systematic reviews [41]. Spin on adverse effects in abstracts of systematic reviews of interventions could be even more damaging for clinical decision making, but its magnitude and consequences have not been assessed in the literature.

**Table 2.** Glossary of terms

| Term | Definition |
|---|---|
| Systematic review | Cochrane [33] defines a systematic review as follows: 'A systematic review attempts to identify, appraise and synthesize all the empirical evidence that meets pre-specified eligibility criteria to answer a specific research question. Researchers conducting systematic reviews use explicit, systematic methods that are selected with a view aimed at minimizing bias, to produce more reliable findings to inform decision making.' |
| Intervention review | Cochrane [33] defines an intervention review as follows: 'Intervention reviews assess the benefits and harms of interventions used in healthcare and health policy.' |
| Orthodontic interventions | Steegmans et al. [34] defined orthodontic interventions as follows: 'Orthodontic interventions refer to the use of any type of orthodontic appliance that are used to move teeth or change the jaw size or position for orthodontic purposes. These interventions also include appliances to maintain or stabilize the results of orthodontic treatment, for example retainers.' |
| Adverse effect | Cochrane [35, 36] defines an adverse effect as 'an adverse event for which the causal relation between the intervention and the event is at least a reasonable possibility'. |
| Spin [3] | 'Distorted presentation of study results'. |
| Spin [3] | 'A misrepresentation of study results, regardless of motive (intentionally or unintentionally) that overemphasizes the beneficial effects of the intervention and overstates safety compared with that shown by the results'. |
| Spin [37] | 'A specific intentional or unintentional reporting that fails to faithfully reflect the nature and range of findings and that could affect the impression the results produce in readers' |
| Spin [38] | 'A specific reporting that fails to faithfully reflect the nature and range of findings and that could affect the impression that the results produce in readers, a way to distort science reporting without actually lying' |
| Misleading reporting related spin [32] | 'Incomplete reporting of the study results that could be misleading for the reader'. |
| Misleading interpretation related spin [32] | Inadequate interpretation of the study results overestimating the beneficial effect of the intervention. |
| Misleading (inappropriate) extrapolation related spin [32] | 'Inappropriate generalization of the study results by inadequate 1) extrapolation from the population, interventions or outcome actually assessed in the study to a larger population, different interventions or outcomes, or 2) inadequate implications for clinical practice. |
| Spin (in the abstract) on adverse effects of interventions [39] | Incomplete or inadequate reporting, interpretation, or extrapolation (or a combination of these variables) of findings on adverse effects of interventions in the abstract that could be misleading for the reader. |

**Why this study is necessary and for who, and what are the objectives of this paper**

Above we reported on the magnitude and the problems associated with incomplete, misleading, and non-assessing and reporting of adverse effects in research studies. In this dissertation we assessed a series of these issues in systematic reviews of orthodontic interventions. Cross-sectional studies were developed, which addressed 12 research questions (Figures 3 and 4).

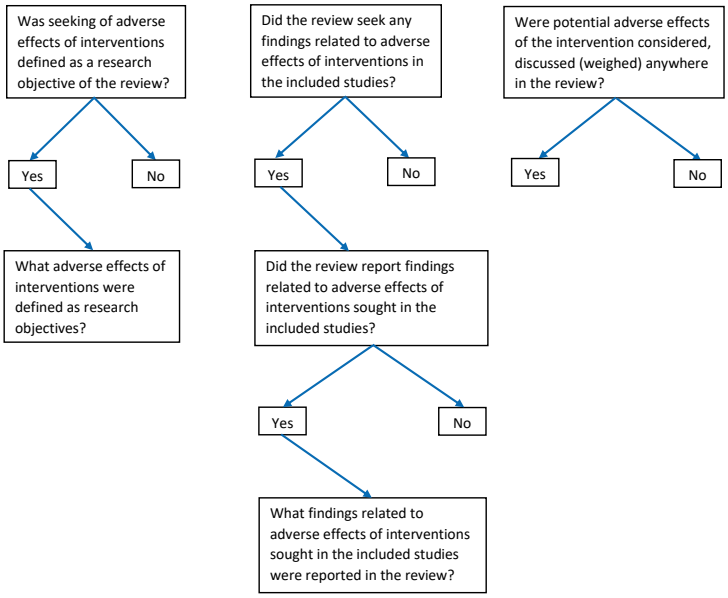


**Figure 3.** Flow diagram "seeking adverse effects of interventions in systematic reviews of orthodontic interventions"

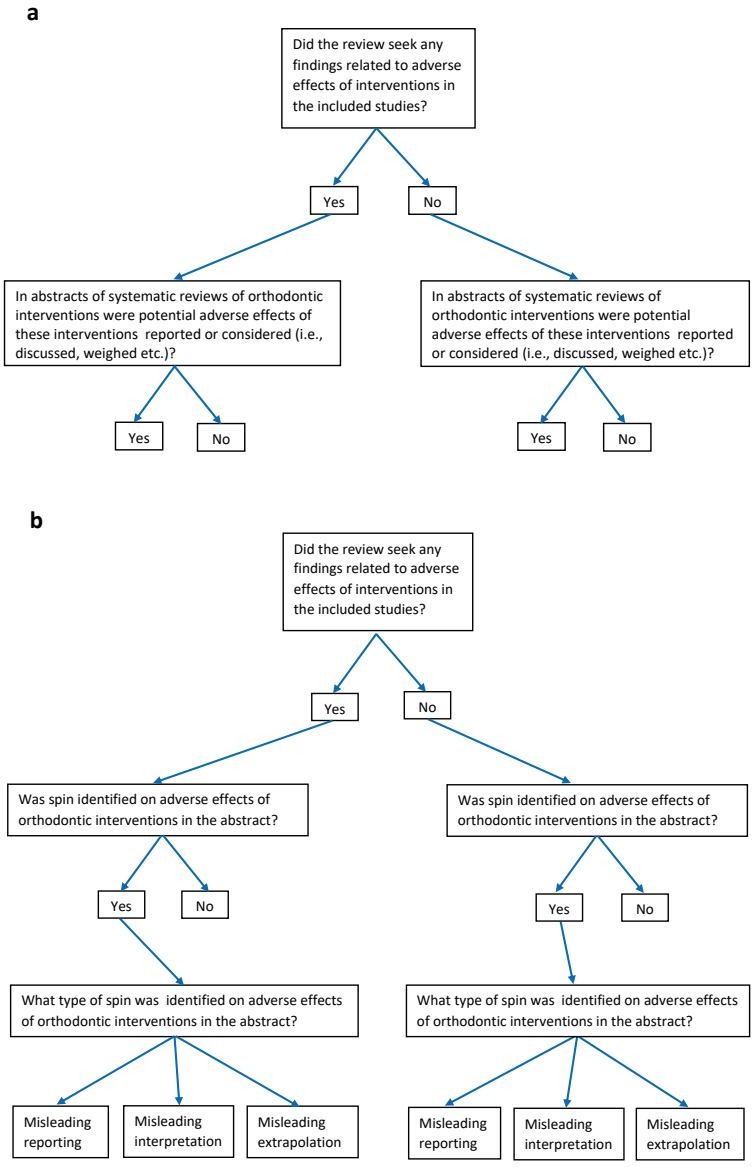


**Figure 4.a.** Reporting or considering adverse effects of orthodontic interventions in the abstract **b.** Spin on adverse effects of orthodontics in the abstract

Our scoping searches showed that these research questions were not assessed previously in the orthodontic literature. Besides our cross-sectional studies, we also explored adverse effects of orthodontic interventions in two critical appraisals and a case report. A detailed list of all research objectives is reported under here. Patients, clinicians, researchers, editors, peer reviewers, guideline developers, policymakers, and research funders, can all benefit from the findings of this dissertation.

**The objectives of this dissertation are:**

1. To assess whether seeking adverse effects was defined as a research objective in systematic reviews of orthodontic interventions (chapters 2 and 3).
2. To assess whether systematic reviews of orthodontic interventions sought any findings related to adverse effects of interventions in the included studies (chapters 2 and 3).
3. To assess whether systematic reviews of orthodontic interventions reported any findings related to adverse effects of interventions sought in the included studies (chapters 2 and 3).
4. To assess whether potential adverse effects of orthodontic interventions were considered, discussed (weighed) anywhere in systematic reviews of orthodontic interventions. (chapters 2 and 3).
5. To assess each type of adverse effect sought in systematic reviews of orthodontic interventions (chapters 2 and 3).
6. To assess whether potential adverse effects were reported or considered (i.e., discussed, weighed, etc.) in abstracts of the systematic reviews of orthodontic interventions (chapters 4 and 5).
7. To assess whether spin was identified on adverse effects of orthodontic interventions in abstracts of systematic reviews of orthodontic interventions (chapters 4 and 5).
8. To assess what type of spin was identified on adverse effects of orthodontic interventions in the abstract of systematic reviews of orthodontic interventions (chapters 4 and 5).
9. To critically appraise a systematic review that assessed the effect of fixed orthodontic retainers on periodontal health [47] (chapter 6).
10. To critically appraise a randomized controlled trial that assessed the post-treatment stability after 5 years of retention with vacuum-formed and bonded retainers [48] (chapter 7).
11. To assess a case with an adverse effect of an orthodontic intervention (chapter 8).

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# CHAPTER 2

## Seeking adverse effects in systematic reviews of orthodontic interventions: protocol for a cross-sectional study

This is a non-edited version of the manuscript:

Steegmans PAJ, Bipat S, Meursinge Reynders RA. Seeking adverse effects in systematic reviews of orthodontic interventions: protocol for a cross-sectional study. Syst Rev. 2019 Apr 5;8(1):89.

## Abstract

**Background:** Before implementing healthcare interventions, clinicians need to weigh the beneficial and adverse effects of interventions. However, a large body of evidence has demonstrated that seeking and reporting of adverse effects is suboptimal in clinical trials and in systematic reviews of interventions. This cross-sectional study will investigate the status of this problem in orthodontics. This study will assess whether adverse effects were sought and whether findings related to adverse effects were reported in systematic reviews of orthodontic interventions in the five leading orthodontic journals and in the Cochrane Database of Systematic Reviews.

**Methods:** Systematic reviews of clinical orthodontic interventions published between 01 August 2009 and 31 July 2019 in the five leading orthodontic journals and in the Cochrane Database will be included. Empty reviews will be excluded. The reporting of outcomes on adverse effects will not determine eligibility, i.e., reviews will not be excluded, because they did not report usable data. Study selection and data extraction will be conducted independently by two authors. Our primary outcome will be the prevalence of systematic reviews of orthodontic interventions that sought any findings related to adverse effects in the included studies. Additional prevalence statistics will be calculated on a series of items related to seeking of adverse effects in the eligible reviews. All statistics will be calculated for (1) all journals together, (2) the group of five orthodontic journals and the Cochrane Database of Systematic Reviews separately, and (3) each individual journal separately. Chi-square tests of independence will be used to compare these groups.

**Discussion:** This study will assess whether adverse effects were sought in systematic reviews of orthodontic interventions. This knowledge is important, because reviews that present an incomplete picture on adverse effects can have unfavorable consequences for the end-users. Also not reporting that no adverse effects were assessed in eligible studies included in a systematic review can mislead pertinent stakeholders. Our findings could have policy implications for making judgments on accepting or rejecting an intervention systematic review for publication, for example, by directing editors and peer-reviewers to adopt the various items on adverse effects defined in the MECIR standards and in the PRISMA harm checklist.

**Keywords:** Orthodontics, Reporting, Systematic review, Interventions, Adverse effect, Adverse event, Harm, Safety, Side effect, Patient-important outcomes

## Background



Making balanced decisions on healthcare interventions requires reliable evidence on both their beneficial and adverse effects. In the Cochrane systematic reviews of interventions, it is therefore mandatory to seek both types of outcomes and include at least one undesirable outcome as a primary outcome measure [1, 2]. In both Cochrane and non-Cochrane reviews of orthodontic interventions, we will assess whether adverse effects were sought and whether findings related to adverse effects were reported.

Since its foundation in 1993, Cochrane has set the standard for medical research-synthesis publications [3]. Systematic reviews with or without meta-analyses are the core of such syntheses and are the foundations for evidence-based practice guidelines and policy. Cochrane reviews of interventions aim at including outcomes that are likely to be important for patients, clinicians, the general public, guideline developers, administrators, and policy makers [2]. Cochrane states: "It is critical that outcomes used to assess adverse effects as well as outcomes used to assess beneficial effects are among those addressed by a review" (chapter 5.4.1) [2]. This issue is important, because a balanced perspective of an intervention can only be obtained when both types of outcomes are assessed and reported with the same rigor. Cochrane has formulated the following definition of an adverse effect: "An adverse event for which the causal relation between the intervention and the event is at least a reasonable possibility" [4, 5]. We adopted Cochrane's definitions of adverse effects, systematic reviews, and interventions reviews in this manuscript (Table 1) [4–6].

Numerous epidemiological studies have shown that adverse effects of interventions are often under-assessed or under-reported in primary research studies [7–11]. In addition, much information on adverse events remains unpublished and the number and range of these events are higher in unpublished compared to published versions of the same study [12]. To improve the reporting of harms in randomized trials, an extension of Consolidated Standards of Reporting Trials (CONSORT) Statement was developed [13]. The reporting of adverse events has improved over time since the publication of this extension, but was still suboptimal for a wide variety of clinical trials [9, 11, 14]. Systematic reviewers have an important role in bringing these issues to the foreground. However, epidemiological studies have shown that seeking and reporting adverse effects of interventions is also suboptimal in systematic reviews [15–18]. In 2016, the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) harm checklist [19] to improve harm reporting in systematic reviews was published, but the consequences of this checklist are still unknown.

In this study, we will assess whether adverse effects were sought and reported in systematic reviews of orthodontic interventions. We will scrutinize such reviews in the five leading orthodontic journals and those registered in the Cochrane Database of Systematic Reviews. Reporting on pain as a result of tooth movement and the various categories of known orthodontic adverse effects as defined by Preoteasa et al. [20] will be assessed in these reviews (Table 2). Scoping searches in the orthodontic literature confirmed the knowledge gaps on our research questions. Our pilot studies on intervention reviews of the Cochrane Database of Systematic Reviews and those published in the five leading orthodontic journals quantified these gaps and further showed the need to undertake this research study. Addressing our research objectives is crucial for patients, clinicians, researchers, policy

makers, and research sponsors. These questions are particularly important, because systematic reviews are increasingly consulted by patients [21].

**Table 1** Glossary of terms

| Term | Definition |
|---|---|
| Systematic review | The Cochrane glossary [5] defines a systematic review as "A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies." |
| Intervention review | Cochrane [6] defines an intervention review as follows: "Intervention reviews assess the benefits and harms of interventions used in healthcare and health policy." |
| Orthodontic interventions | Orthodontic interventions refer to the use of any type of orthodontic appliances that are used to move teeth or change the jaw size or position for orthodontic purposes. These interventions also include appliances to maintain or stabilize the results of orthodontic treatment, for example retainers. |
| Adverse effect | Cochrane [4, 5] defines an adverse effect as "an adverse event for which the causal relation between the intervention and the event is at least a reasonable possibility." |

**Table 2** Adverse effects hypothetically linked to orthodontic interventions [20]

| Subgroup | Description |
|---|---|
| Local adverse effects | |
| Dental | • Crown: decalcifications, decays, tooth wear, enamel cracks and fractures; discolorations, deterioration of prosthetic crown (as fracturing a ceramic one during debonding)<br>• Root: root resorption, early closure of root apex, ankylosis<br>• Pulp: ischemia, pulpitis, necrosis |
| Periodontal | • Gingivitis, periodontitis, gingival recession or hypertrophy, alveolar bone loss, dehiscences, fenestrations, interdental fold, dark triangles |
| Temporomandibular joint | • Condylar resorption, temporomandibular dysfunction |
| Soft tissues of the oral and maxillofacial region | • Trauma (e.g., long archwires, headgear related), mucosal ulcerations or hyperplasia, chemical burns (e.g., etching related), thermal injuries (e.g., overheated burs), stomatitis, clumsy handling of dental instruments |
| Unsatisfactory treatment outcome | • Inadequate morpho-functional, esthetic or functional final result, relapse, failure to complete treatment due to treatment dropout |
| Systemic adverse effects | |
| Psychological | • Teasing, behavioral changes of patients and parents; discomfort associated with pain presence and esthetic look discontents during orthodontic appliance usage |
| Gastro-intestinal | • Accidental swallowing of small parts of the orthodontic device (tubes, brackets) |
| Allergies | • To nickel or latex |
| Cardiac | • Infective endocarditis |
| Chronic fatigue syndrome | |
| Cross infections | • From doctor to patient, patient to doctor, patient to patient |

## Objectives

The main research question of this cross-sectional study is the following: “Do reviewers seek adverse effects in systematic reviews of orthodontic interventions?” To address this question, we have defined the following objectives:

- To calculate the prevalence of eligible systematic reviews of orthodontic interventions that defined seeking of adverse effects as a research objective of the review
- To calculate the prevalence of eligible systematic reviews of orthodontic interventions that sought any findings related to adverse effects in the included studies
- To calculate the prevalence of eligible systematic reviews of orthodontic interventions that considered and discussed (weighed) potential adverse effects of the intervention anywhere in the review
- To calculate the prevalence of each type of adverse effect sought in the review

## Methods

We used the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) 2015 statement as the guideline for reporting this protocol [22, 23]. The PRISMA-P checklist is included as Additional file 1. Figure 1 represents the flow diagram of our research methods. Our first step was to conduct scoping searches to identify knowledge gaps and prioritize research questions on seeking and reporting of adverse effects in systematic reviews of orthodontic interventions. Two reviewers (PS and RMR) subsequently conducted pilot tests to assess the validity of these questions and the research methods and to fine-tune them. The sample size for the pilot test was calculated a priori [24], and random numbers were generated to select pilot systematic reviews [25]. The procedures for our pilot tests are reported in Additional file 2. In the following sections, we presented our planned methods based on these pilot tests.

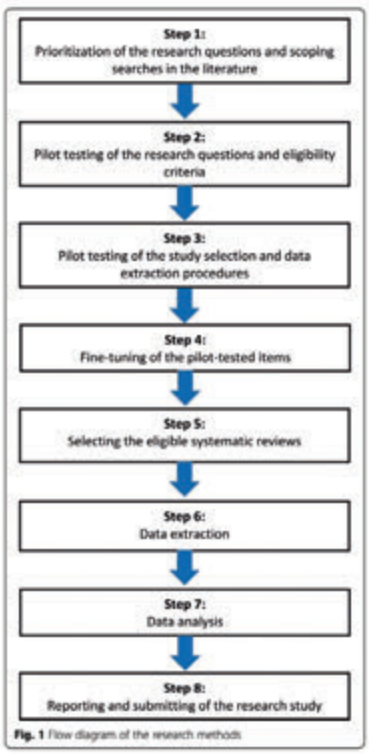

**Fig. 1** Flow diagram of the research methods

**Eligibility criteria**

***Study designs***

- We will include systematic reviews of orthodontic interventions. The definition of a systematic review, an intervention review, and orthodontic interventions listed in the Glossary of terms will be used to assess whether a review is eligible (Table 1).
- We will exclude (1) non-interventional reviews such as "Methodology," "Diagnostic," "Qualitative," and "Prognostic"; (2) rapid and scoping reviews; (3) systematic reviews that focus exclusively on adverse effects of interventions; and (4) systematic reviews of interventions that did not find any eligible studies (empty reviews).

***Participants***

- We will include systematic reviews on any type of patients undergoing orthodontic interventions, i.e., patients of any health status, sex, age, demographics, and socio-economic status.
- We will exclude (1) intervention reviews that focus exclusively on patients with congenital anomalies, for example, with cleft lip and palate, and (2) systematic reviews of animal or laboratory studies.

***Interventions***

- We will include the following: (1) Systematic reviews that assess the effects of clinical orthodontic interventions. Clinical orthodontic interventions refer to the use of any type of orthodontic appliances that are used to move teeth or change the jaw size or position for orthodontic purposes. (2) Systematic reviews of interventions with appliances to maintain or stabilize the results of orthodontic treatment, for example, retainers. (3) Systematic reviews of orthodontic interventions that compare the effects of orthodontic treatment with or without additional interventions such as pharmacological or small surgical procedures, e.g., periodontal or implant surgery.
- We will exclude (1) systematic reviews in which patients receive orthodontic treatment, but in which the effects of other interventions, e.g., periodontal surgery, are compared and not the effects of orthodontic interventions; (2) systematic reviews of interventions in which orthodontic appliances are specifically used for other purposes, e.g., changing jaw positions to treat respiration or temporomandibular disorders; and (3) systematic reviews of orthodontic interventions that included orthognathic surgery.
- No exclusion criteria will be applied to the characteristics of the operator who conducted the interventions.

***Outcomes***

- Any adverse effect of an orthodontic intervention scored at any endpoint or timing will be eligible.
- The effects of orthodontic interventions do not refer just to outcomes related to tooth and jaw size and positions, but also to broader outcomes such as periodontal

health, esthetic changes, the health of the temporomandibular joint, patient health experiences, and economic issues associated with the intervention.
- The reporting of outcomes on adverse effects will not determine the eligibility of reviews for this cross- sectional study, i.e., reviews will not be excluded because they did not provide “usable” data [2].



***Setting***

- No exclusion criteria will be applied to the type of setting, e.g., university or private practice, etc., in which the interventions were conducted.

**Information sources**

We will manually search eligible systematic reviews between 01 August 2009 and 31 July 2019 in the Cochrane Database of Systematic Reviews [26] and in the websites of the five leading orthodontic journals. We consulted the journal citation reports by Clarivate Analytics [27] to identify the five leading orthodontic journals based on their impact factor. Based on these reports, the following orthodontic journals were included: European Journal of Orthodontics [EJO], American Journal of Orthodontics and Dentofacial Orthopedics [AJODO], Angle Orthodontist, The Korean Journal of Orthodontics, and Orthodontics and Craniofacial Research. Recently launched orthodontic journals, i.e., covering less than 10 years of journal publication, will not be eligible. The first of August 2009 was chosen as the incept data for our searches, because it coincides with the launch of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement and guidance on 21 July 2009 [28, 29].

**Study records**

***Data management***

- All study selection and data extraction procedures will be conducted by two authors (PS and RMR) independently.
- Our pilot tests were also used to train both reviewers in applying our methods consistently and to calibrate them [23].
- Disagreement on the eligibility of a paper or the extraction of data will be resolved through (1) discussions between reviewers, (2) rereading the pertinent paper, or (3) contacting its authors by email [28]. Persistent disagreements will be resolved through the consultation of a methodologist (SB).
- All eligible systematic reviews will be downloaded as PDFs, and all data will be extracted to an Excel spreadsheet [30].

***Selection process***

- All titles and abstracts will be screened for eligibility in the websites of the five orthodontic journals. We will search the section "Dentistry and Oral health" for eligible reviews in the Cochrane Database of Systematic Reviews [26].
- When updates of reviews are identified, we will only consider the latest version.
- Authors suspect of multiple publications of the same systematic review will be contacted by email. We plan to consider the first publication, but this decision will be weighed on a case-by-case basis. Our rationale for these decisions will be reported in the completed study.
- A PRISMA flow diagram will illustrate our selection procedures [28, 29].
- All eligible and excluded systematic reviews will be presented in tables. The rationale for exclusion will be listed for each excluded review.

***Data collection process***

- Eligible studies and their pertinent supplemental files will be merged into binder PDFs, and multiple search terms will be applied to facilitate data extraction [31, 32].
- We consulted various articles on adverse effects [4, 13, 18, 19, 33, 34] and thesauri to develop these search terms. A table with all search terms is listed in Additional file 3.
- All pertinent data items will be extracted using our pilot tested data collection forms. These forms are presented in Additional file 4 and incorporate all our research questions. We consulted the PRISMA [28, 29] and the PRISMA-P [22, 23] checklists to develop these data collection forms.
- Criteria for scoring the pertinent data items are defined in these forms.
- We will search the entire eligible review, i.e., the text, tables, figures, and supplemental files. The plain language summary in eligible Cochrane systematic reviews will not be scrutinized for data items.
- Modifications made in the collection forms during data extraction will be reported in the section "Differences between the protocol and review" together with the rationale for these changes.

***Scoring adverse effects of orthodontic interventions***

- We will adopt a priori the various categories of known orthodontic adverse effects as defined by Preoteasa et al. [20], which were divided into two main types: local and systemic, with their pertinent subtypes (Table 2).
- We will also consider pain as a result of tooth movement and additional adverse effects of orthodontic interventions that are identified post hoc, i.e., during data extraction, and are not listed in Table 2. We will explain the rationale for including specific additional effects as adverse and will produce a framework for categorizing them.
- Ambiguous outcomes that could be interpreted as either beneficial or adverse will not be scored as "adverse." We will also present the rationale for this score.

Ambiguous outcomes will only be scored as adverse when the authors of the pertinent review define these outcomes as such.



**Outcomes and statistical analyses**

- All research questions are presented in flow diagrams (Fig. 2).
- All planned outcomes are presented in a summary of findings table (Table 3).
- All prevalence data will be calculated and reported with their 95% confidence levels.
- Prevalence statistics will be calculated for (1) all journals together, (2) the group of five orthodontic journals and the Cochrane Database of Systematic Reviews separately, and (3) each individual journal separately. Comparisons between these statistics will be calculated. These statistics will be compared with chi-square tests of independence. We will report the value of chi-square, the degrees of freedom (df), and the p value. A p value of $< 0.05$ will be considered to be statistically significant. We will use Stata software (Stata Corporation, College Station, TX, USA) version 15 for all the statistical analyses [35].
- We will report all outcomes that will be introduced or eliminated post hoc together with the rationale for inclusion or exclusion.

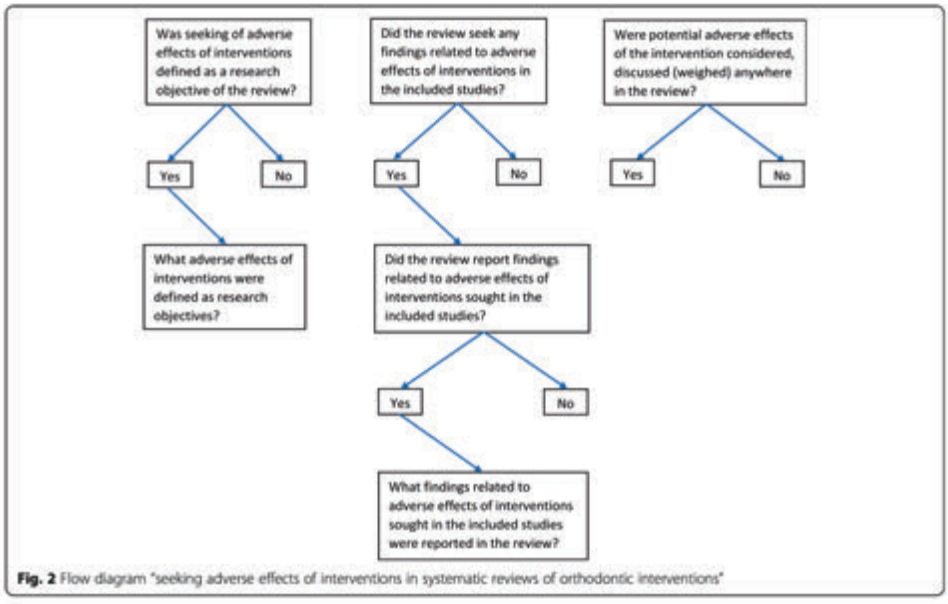


**Fig. 2** Flow diagram "seeking adverse effects of interventions in systematic reviews of orthodontic interventions"

**Table 3** Summary of findings

| Description of outcomes from the main text | Statistic |
|---|---|
| The number of retrieved systematic reviews | Number |
| The prevalence of eligible systematic reviews of orthodontic interventions | Prevalence |
| The prevalence of eligible systematic reviews of orthodontic interventions that defined seeking of adverse effects of interventions as a research objective of the review | Prevalence |
| The prevalence of eligible systematic reviews of orthodontic interventions that sought any findings related to adverse effects of interventions in the included studies | Prevalence |
| The prevalence of eligible systematic reviews of orthodontic interventions that reported findings related to the adverse effects of interventions sought in the included studies | Prevalence |
| The prevalence of eligible systematic reviews of orthodontic interventions that considered, discussed (weighed) potential adverse effects of the intervention anywhere in the review | Prevalence |
| The prevalence of each type of adverse effect of interventions defined in the objectives of the review | Prevalence |
| The prevalence of each type of adverse effect of interventions sought in the review | Prevalence |

**All prevalence data will be presented with their 95% confidence intervals**

**Reporting of the research study and data management**

- We will adopt The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement as the guideline for reporting the completed cross-sectional study [36].
- We prepared a data management plan for the long- term storage of our research data [37]. This plan guarantees that (1) all our project data will be made freely available and (2) our submitted article will be accompanied by additional files with all raw data of the completed study or with a link to a repository where these files will be deposited. In the latter case, we will register our repository in the Registry of Research Data Repositories [38]. (3) Our project data will be presented in a format that permits other scientists to understand, cite, and reuse the data. (4) Sensitive data will be protected. (5) Our data management plan will be frequently reassessed and updated if necessary [37, 38].

**Differences between the protocol and the completed study**

All differences between the protocol and the final research study will be reported together with the rationale for these changes. We will also present the consequences of these modifications on the magnitude, direction, and validity of the outcomes [39].

## Discussion

### Strengths

We point at four key strengths of this research study. First, extensive scoping searches and pilot studies were conducted to fine-tune our research questions and procedures. Our pilot studies also confirmed the importance of our research questions. Second, the research team consisted of two topic experts (PS and RMR) and two methodologists (RMR and SB). Third, all study selection and data extraction procedures were conducted by two operators (PS and RMR) independently. Fourth, this study will permit reproducibility, because we will publish the protocol a priori and all raw data of the completed study will be reported in additional files or will be deposited in an open access repository [37, 40].

### Limitations

The limitations of this research study include the following: (1) It does not cover all journals that have published orthodontic intervention systematic reviews, but only a subgroup, i.e., those published in the five leading orthodontic journals and in the Cochrane Database of Systematic Reviews. However, we expect that the choice of this subgroup of the leading orthodontic literature will produce outcomes that will underestimate the true severity of the problem. (2) Including only systematic reviews of orthodontic interventions published in the last 10 years could introduce the risk of publication bias. However, we chose this period, because it will represent the actual knowledge status on assessing adverse effects in orthodontic intervention systematic reviews. Further, this period coincides with the launch in 2009 of the PRISMA reporting checklist, which is an important update on how to report items in systematic reviews [28, 29].

### Importance and beneficiaries

In this research study, we will assess whether adverse effects were sought and reported in both Cochrane and non-Cochrane systematic reviews of orthodontic interventions. This is important, because of the following: (1) The validity of the findings of systematic reviews of interventions depends on a balanced presentation of both the benefits and adverse effects of the intervention [19]. (2) There is a large body of evidence that has demonstrated that seeking and reporting of adverse effects is suboptimal in a wide variety of clinical trials [7–11]. Systematic reviewers can have a crucial role as whistle blowers by bringing these knowledge gaps to the foreground. However, their position can also be damaging, because reviews that present an incomplete picture on these gaps can have unfavorable consequences for the end-users. For example, not reporting that no adverse effects were assessed in eligible studies included in a systematic review can mislead readers.

Our findings could have policy implications for making judgments on accepting or rejecting a systematic reviews of orthodontic interventions for publication, for example, by directing editors and peer-reviewers to adopt the various items on adverse effects defined in the Methodological Expectations of Cochrane Intervention Reviews (MECIR) standards [1] and the PRISMA harm checklist [19]. Patients, clinicians, researchers, editors, peer-reviewers,

guideline developers, policy makers, and research funders will all benefit from the findings of this research study.

## Additional files

**Additional file 1:** Checklist for the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. (DOCX 33 kb)
**Additional file 2:** Pilot tests. (DOCX 21 kb)
**Additional file 3:** Search terms and their derivatives. (DOCX 15 kb)
**Additional file 4:** Data collection forms. (DOCX 16 kb)

**Abbreviations**
EQUATOR Network: Enhancing the Quality and Transparency Of health Research Network;
MECIR: Methodological Expectations of Cochrane Intervention Reviews;
PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses;
PRISMA-P: Preferred Reporting Items for Systematic review and Meta-Analysis-Protocols

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All expenses for preparing this protocol and for conducting the subsequent research study will be paid evenly by each author.

**Availability of data and materials**
Not applicable

**Authors' contributions**
PS and RMR conceived and designed the study protocol for this cross- sectional study. RMR is the guarantor. PS and RMR conducted the pilot testing of the study selection procedures and data extraction forms and fine-tuned the research protocol after the pilot testing. SB provided support on methodological and statistical issues and assisted in the overall fine-tuning of this protocol. All authors read and approved the final protocol.

**Ethics approval and consent to participate**
Not applicable

**Consent for publication**
Not applicable

**Competing interests**
Reint Meursinge Reynders and Shandra Bipat are both Associate Editors for Systematic Reviews. The authors declare that they have no competing interests.

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# CHAPTER 3

## Seeking adverse effects in systematic reviews of orthodontic interventions: a cross-sectional study (part 1)

This is a non-edited version of the manuscript:

Steegmans PAJ, Di Girolamo N, Bipat S, Reynders RAM. Seeking adverse effects in systematic reviews of orthodontic interventions: a cross-sectional study (part 1). Syst Rev. 2023 Jul 3;12(1):112.

## Abstract

**Background** Systematic reviews that assess the benefits of interventions often do not completely capture all dimensions of the adverse effects. This cross-sectional study (part 1 of 2 studies) assessed whether adverse effects were sought, whether the findings on these effects were reported, and what types of adverse effects were identified in systematic reviews of orthodontic interventions.

**Methods** Systematic reviews of orthodontic interventions on human patients of any health status, sex, age, and demographics, and socio-economic status, in any type of setting assessing any type of adverse effect scored at any endpoint or timing were eligible. The Cochrane Database of Systematic Reviews and 5 leading orthodontic journals were manually searched for eligible reviews between August 1 2009 and July 31 2021. Study selection and data extraction was conducted by two researchers independently. Prevalence proportions were calculated for four outcomes on seeking and reporting of adverse effects of orthodontic interventions. Univariable logistic regression models were used to determine the association between each one of these outcomes and the journal in which the systematic review was published using the eligible Cochrane reviews as reference.

**Results** Ninety-eight eligible systematic reviews were identified. 35.7% (35/98) of reviews defined seeking of adverse effects as a research objective, 85.7% (84/98) sought adverse effects, 84.7% (83/98) reported findings related to adverse effects, and 90.8% (89/98) considered or discussed potential adverse effects in the review. Reviews in the journal Orthodontics and Craniofacial Research compared with Cochrane reviews had approximately 7 times the odds (OR 7.20, 95% CI 1.08 to 47.96) to define seeking of adverse effects in the research objectives. Five of the 12 categories of adverse effects accounted for 83.1% (162/195) of all adverse effects sought and reported.

**Conclusions** Although the majority of included reviews sought and reported adverse effects of orthodontic interventions, end-users of these reviews should beware that these findings do not give the complete spectrum on these effects and that they could be jeopardized by the risk of non-systematically assessing and reporting of adverse effects in these reviews and in the primary studies that feed them. Much research is ahead such as developing core outcome sets on adverse effects of interventions for both primary studies and systematic reviews.

**Keywords** Orthodontics, Reporting, Systematic review, Interventions, Adverse effect, Adverse event, Harm, Safety, Side effect, Patient important outcomes

## Background

To get a balanced perspective of an intervention, systematic reviewers need to report both its beneficial and adverse effects [1]. In this cross-sectional study we assessed whether adverse effects were sought, whether the findings on these effects were reported, and what types of adverse effects were identified in systematic reviews published in the Cochrane Database of Systematic reviews [2] and in 5 leading orthodontic journals.



'Cochrane defines an adverse effect as 'an adverse event for which the causal relation between the intervention and the event is at least a reasonable possibility' [3, 4]. This definition and other key terms used in this manuscript are listed in Table 1 [5, 6]. A wide body of epidemiological studies has shown that adverse effects of interventions in primary research studies are often under-assessed, and/or under-reported, and/or distorted [7–13]. These issues can misinform anyone trying to make valid decisions on a healthcare intervention. An extension of the Consolidated Standards of Reporting Trials (CONSORT) Statement was developed to tackle poor reporting of harms in randomized trials [14]. Since the publication of this statement, the reporting of adverse events in clinical trials has improved, but is still suboptimal [10, 12, 15, 16].

Systematic reviews could provide even more information on adverse effects, because they assess large amounts of data from a wide spectrum of sources (possibly including both published and unpublished data). By assessing the data of multiple single studies, systematic reviewers can make a more balanced assessment of an intervention. This is an important issue, because serious adverse effects may occur rarely and might be missed in single studies. However, epidemiological research showed that the seeking and reporting of adverse effects of interventions and the methods used to identify and synthesize them [17–21] were also poor in systematic reviews. The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) harms checklist was published in 2016 [22] to improve harms reporting in systematic reviews, but its consequences are still largely unknown.

We performed 2 cross-sectional studies on assessing and reporting of adverse effects in systematic reviews of orthodontic interventions. In this study (part 1), we assessed whether adverse effects were sought and reported and what findings on these adverse effects were reported in systematic reviews of orthodontic interventions published in the Cochrane Database of Systematic reviews [2] and in 5 leading orthodontic journals. In a second study (part 2) we assessed the reporting on adverse effects and the presence of spin on adverse effects in the abstracts of these reviews [23]. Adverse effects of orthodontic interventions refer to for example, pain associated with orthodontic tooth movement, root resorption, decalcifications, periodontal problems, relapse, and undesired health experiences [24]. Recent (November 22 2021) scoping searches confirmed that our research objectives have not been addressed previously.

**Table 1** Glossary of terms

| Term | Definition |
|---|---|
| Systematic review | Cochrane [5] defines a systematic review as follows: 'A systematic review attempts to identify, appraise and synthesize all the empirical evidence that meets pre-specified eligibility criteria to answer a specific research question. Researchers conducting systematic reviews use explicit, systematic methods that are selected with a view aimed at minimizing bias, to produce more reliable findings to inform decision making.' |
| Intervention review | Cochrane [5] defines an intervention review as follows: 'Intervention reviews assess the benefits and harms of interventions used in healthcare and health policy.' |
| Orthodontic interventions | Steegmans et al. [6] defined orthodontic interventions as follows: 'Orthodontic interventions refer to the use of any type of orthodontic appliance to move teeth or change the jaw size or position for orthodontic purposes. These interventions also include appliances to maintain or stabilize the results of orthodontic treatment, for example retainers.' |
| Adverse effect | Cochrane [3, 4], defines an adverse effect as 'an adverse event for which the causal relation between the intervention and the event is at least a reasonable possibility' |

## Objectives

The objectives of this research study are formulated in the following four research questions:

1) Was seeking of adverse effects of interventions defined as a research objective of the review?

2) Did the review seek any findings related to adverse effects of interventions in the included studies?

3) Did the review report findings related to adverse effects of interventions sought in the included studies?

4) Were potential adverse effects of the intervention considered, discussed (weighed) anywhere in the review?

We also assessed what adverse effects of interventions were defined as research objectives and what adverse effects of interventions were sought and reported in the review.

## Methods

The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [25] and the PRISMA 2020 statement [26, 27] were consulted for reporting this cross-sectional study. The STROBE checklist of items for reporting cross-sectional studies was presented in Additional file 1. The methods for this cross-sectional study were explained in our published protocol [6] and can be consulted through the following link https://systematicreviewsjournal.biome dcentral.com/articles/10.1186/s13643-019-1000-1. We adopted the framework of this protocol to report the methods section of this study and its additional files. Raw data are recorded in Open Science Framework (https://osf.io/ka7mp/). Differences between methods originally planned in the protocol and those implemented in the final research study were given with the rationales for these differences in Additional file 2. No patients were involved in the development of the protocol or in the conduct of this study.

**Eligibility criteria**

The eligibility criteria have been published previously [6, 28] and are presented again in Table 2 [29].

**Table 2** Eligibility criteria

| Item | Included | Excluded |
|---|---|---|
| Study designs | Systematic reviews of orthodontic interventions. The definition of systematic review, intervention review, and orthodontic interventions listed in the Glossary of terms will be used to assess whether a review is eligible (Table 1) | 1) Non-interventional reviews such as, 'Methodology', 'Diagnostic', 'Qualitative', 'Prognostic' etc<br>2) Rapid and scoping reviews<br>3) Systematic reviews with Bayesian network meta-analysis<br>5) Systematic reviews of interventions that did not find any eligible studies (empty reviews) |
| Participants | Systematic reviews on any type of patients undergoing orthodontic interventions, i.e., patients of any health status, sex, age, and demographics, and socio-economic status | 1) Intervention reviews that focus exclusively on patients with congenital anomalies, for example with cleft lip and palate<br>2) Systematic reviews of animal or laboratory studies |
| Interventions | 1) Systematic reviews that assessed the effects of clinical orthodontic interventions. Clinical orthodontic interventions refer to the use of any type of orthodontic appliance that are used to move teeth or change the jaw size or position for orthodontic purposes<br>2) Systematic reviews of interventions with appliances to maintain or stabilize the outcomes of orthodontic treatment, for example retainers<br>3) Systematic reviews of orthodontic interventions that compared the effects of orthodontic treatment with or without additional interventions such as pharmacological or small surgical interventions, e.g., periodontal or implant surgery<br>4) No exclusion criteria were applied to the characteristics of the operator who conducted the interventions | 1) Systematic reviews in which patients receive orthodontic treatment, but in which the effects of other interventions, e.g., periodontal surgery, were compared and not the effects of orthodontic interventions<br>2) Systematic reviews of interventions in which orthodontic appliances were specifically used for other purposes, e.g., changing jaw positions to treat respiration or temporomandibular disorders<br>3) Systematic review of orthodontic interventions that included orthognathic surgery<br>4) Systematic reviews that focussed exclusively on adverse effects of interventions<br>5) Systematic reviews that did not assess a specific orthodontic intervention, but referred to orthodontic treatment as a whole |
| Outcomes | 1) Any adverse effect of orthodontic interventions scored at any endpoint or timing<br>2) The effects of orthodontic interventions did not refer just to outcomes related to tooth and jaw size and positions, but also to broader outcomes such as periodontal health, esthetic changes, the health of the temporomandibular joint, patient health experiences, and economic issues associated with the interventions<br>3) The reporting of outcomes on adverse effects did not determine eligibility of reviews for this cross-sectional study, i.e., reviews were not excluded because they did not report measured outcome data in a 'usable' way [29] | No exclusion criteria |
| Stetting | Any type of setting in which the interventions were conducted, i.e., university or private practice | No exclusion criteria |

**Information sources and search strategy**

The information sources for this study were the Cochrane Database of Systematic Reviews [2] and the websites of 5 leading orthodontic journals. The selection of these 5 orthodontic journals was based on having been published at least 10 years and the highest impact factor [30]. The impact factor in 2018, i.e., the year when the protocol was developed, was used to select these journals. The 5 selected orthodontic journals are: European Journal of Orthodontics [EJO], American Journal of Orthodontics and Dentofacial Orthopedics [AJODO], Angle Orthodontist (AO), The Korean Journal of Orthodontics (KJO), and Orthodontics and Craniofacial Research (O&CR). The impact factors of these journals are listed in Additional file 2. August 1 2009 was chosen as the inception date for searching the information sources, because it coincides with the publication of the PRISMA statement and guidance document on 21 July 2009 [31, 32]. Eligible systematic reviews were manually searched in these information sources from the inception date until July 31 2021.

**Study records**

***Data management***

All study selection and data extraction procedures were conducted independently by 2 authors (PS and RMR). Pilot tests were done a priori to train and calibrate these operators [33]. Disagreements between these reviewers during these study selection and data collection were resolved in the following order: Firstly, through discussions; secondly, through rereading the article in question; and thirdly, through contacting of the authors of the pertinent manuscript by email to obtain additional information that could help with decision-making [27]. Persistent disagreements were resolved through discussions with a methodologist (SB). All eligible systematic reviews with their supplementary files were downloaded as PDFs and merged in binder files [34, 35]. Data were collected in an Excel spreadsheet [36].

***Study selection and data collection procedures***

Titles and abstracts were screened for eligible reviews in the websites of the 5 selected orthodontic journals. Eligible Cochrane reviews were searched in the 'Dentistry and Oral health' section of the Cochrane Database of Systematic Reviews [2]. When Cochrane reviews were updated, we only considered the latest published version. A PRISMA flow diagram was presented to illustrate the selection process of the eligible reviews [26, 27]. All included studies and excluded studies were reported and the rationales for exclusion were given in Additional file 3. Contacting of authors was not necessary to clarify eligibility or data extraction issues. We used our pilot tested data collection forms for the extraction of all pertinent data items. These forms are presented in Additional file 2. The entire eligible review except the abstract and protocol were searched, i.e., the main text, tables, figures, and supplemental files. This strategy was implemented for all eligible reviews. In Cochrane systematic reviews, we also did not search data items in the plain language summary.

**Assigning adverse effects of orthodontic interventions**

Cochrane defines an adverse effect as 'an adverse event for which the causal relation between the intervention and the event is at least a reasonable possibility' [3, 4]. These events can have a permanent or temporary adverse effect on the health condition of the patient. Root resorption, decalcifications of enamel or caries around orthodontic appliances are well known permanent adverse effects of orthodontic interventions, while pain and discomfort during tooth movement are generally temporary adverse effects. Events associated with orthodontic interventions that could have an adverse effect on the health condition were also labeled as adverse events, e.g., breaking of appliances, failure to complete treatment, and tolerability of orthodontic appliances.

According to our protocol we adopted the framework of known orthodontic adverse effects as reported previously by Preoteasa et al. [24] (Additional file 2) and made some changes in labeling the headings of the various categories of adverse effects (Additional file 2). A total of 12 categories of adverse effects were defined. Additional adverse effects identified during our data extraction procedures were also included in this framework and when ambiguous

the rationale for including these adverse effects was given. The following types of adverse events were not labeled as adverse effects: (1) effects that do not refer to health conditions and could be ambiguous, e.g., costs, duration of treatment, number of appointments etc. (2) effects that refer to pre-existing health problems that can actually improve as a result of the intervention, e.g., respiratory problems as a result of maxillary expansion or self-esteem as a result of the retraction of protruding maxillary incisors.

**Power calculation**

Epitools epidemiological software was used to calculate the required sample size of eligible systematic reviews of orthodontic interventions [37]. We calculated the required sample size of 73 reviews based on the following input: estimated proportion 0.25, desired precision 0.1, and confidence level 0.95. The estimated proportion was based on the findings in our pilot tests as reported in our protocol [6]. These pilot test showed that findings related to adverse effects were sought in 3 of 12 systematic reviews on orthodontic interventions representing the estimated proportion of 0.25 (3/12).

**Outcomes and statistical analyses**

We reported the number of retrieved systematic reviews and eligible reviews and calculated the prevalence proportions that addressed our research questions. All outcomes were calculated as originally planned in our published protocol [6]. Prevalence proportions were calculated for: (1) all journals together (2) each journal separately and (3) the group of 5 leading orthodontic journals together and the Cochrane reviews separately. Univariable logistic regression models were built to determine the association between each one of four outcomes and the journal in which the systematic review was published, using the Cochrane Database of Systematic reviews as reference. The strength of association was quantified using odds ratios (OR), and 95% confidence intervals (95% CI). Analyses were performed with the use of commercial software (IBM SPSS 22.0, SPSS Inc, Chicago, IL). A two-sided *P* value of 0.05 was considered to be statistically significant.

## Results

**Results of the search**

Through our searches in the databases of the Cochrane Database of Systematic reviews and the 5 leading orthodontic journals we identified 324 reports. One Cochrane review was excluded, because it was later updated leaving 323 reports for screening. A total of 180 papers was excluded during the title and abstract screening and 45 during full text screening. A total of 98 systematic reviews fulfilled the eligibility criteria of this study. The results of the individual selection steps are presented in a PRISMA flow diagram (Fig. 1) [26, 27]. All included studies are listed in Additional file 3 and excluded studies with the rationale for their exclusion are given in Additional file 4.

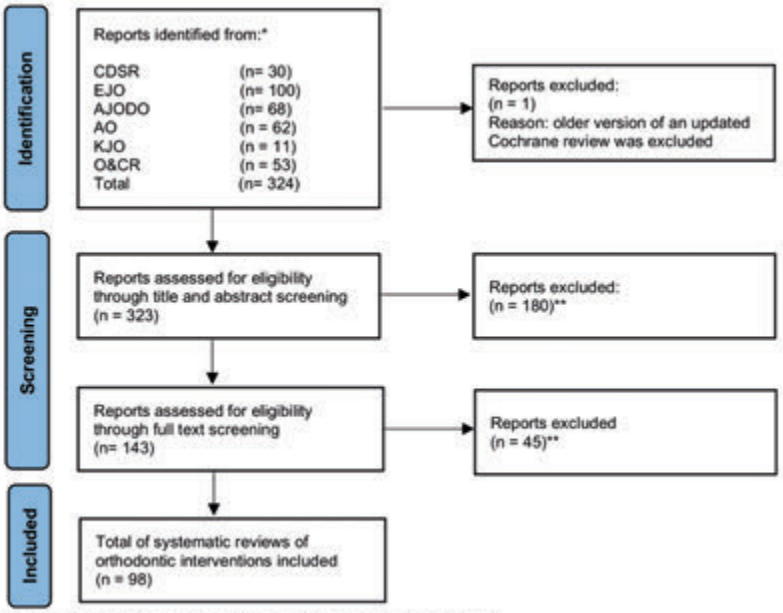


**Fig. 1** Flow diagram for the selection of systematic reviews of orthodontic interventions

**Included studies**

Figure 2 presents the number of eligible systematic reviews of orthodontic interventions published during the eligible time span. Table 3 presents the number of eligible reviews for each selected journal and shows that 72.4% (71/98) of the included reviews came from the EJO, AJODO, and AO. Table 3 also gives the types of orthodontic interventions for each of these journals, which are divided in three categories. Category 1 refers to orthodontic interventions to move teeth modify jaws such as fixed orthodontic appliances or palatal expansion appliances. Category 2 refers to orthodontic interventions that also include additional surgical, pharmacological or vibrational interventions such as mini-implants, prostaglandins, piezo surgery, or vibratory stimulation. Category 3 refers to orthodontic interventions with appliances to maintain or stabilize orthodontic treatment results such as retainers. The majority of included reviews, 70.4% (69/98), assessed orthodontic interventions to move teeth or modify jaws and 28.6% (28/98) assessed orthodontic interventions with additional surgical, pharmacological or vibratory interventions.

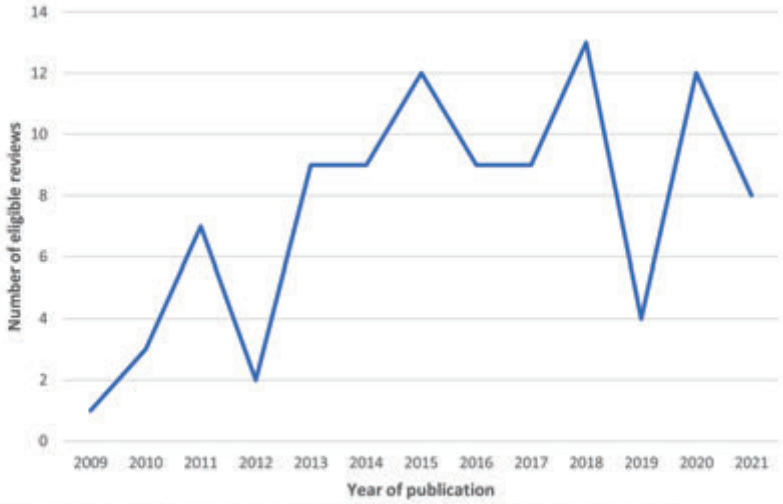


**Fig. 2** Line chart of the number of eligible systematic reviews published between August 1 2009 and July 31 2021

**Table 3** Characteristics of included reviews

| Type of orthodontic intervention | Cochrane | EJO | AJODO | AO | KJO | O&CR | Total |
|---|---|---|---|---|---|---|---|
| Category 1. Orthodontic interventions to move teeth or modify jaws | 7 | 21 | 14 | 15 | 2 | 10 | 69 |
| Category 2. Orthodontic interventions with additional surgical, pharmacological or vibratory interventions | 3 | 6 | 6 | 8 | 1 | 4 | 28 |
| Category 3. Orthodontic interventions to maintain or stabilize orthodontic results | 0 | 1 | 0 | 0 | | 0 | 1 |
| Total | 10 | 28 | 20 | 23 | 3 | 14 | 98 |

**Outcomes to the research questions**

Figure 3 presents the answers to each individual research question and Table 4 gives the proportions. We reported the proportions in answering the four research questions over time in Table 5. The prevalence of reviews that defined seeking of adverse effects of interventions as a research objective was low, i.e., 35.7% in the 98 eligible reviews. Instead, the proportions that addressed the other 3 research question were 85% and higher indicating that seeking and reporting of findings related to adverse effects of interventions in the included studies and considering or discussing potential adverse effects anywhere in the review were implemented in most of the eligible reviews. As compared to the Cochrane Database of Systematic Reviews, the journal of Orthodontics and Craniofacial research had approximately 7 times the odds (OR 7.20, 95%CI 1.08 to 47.96) to report that adverse effects were sought in the research objectives. The other journals were not significantly more likely to report that adverse effects were sought in the research objectives (Table 6). For the other 3 outcomes, no statistical analysis was performed considering the low variability in the response scored (prevalence of 'no' ranging from 9.2 to 15.3%) and the overall small sample sizes (Table 4).

**Labeling adverse effects of orthodontic interventions**

The type of adverse effects most frequently defined as research objectives were adverse effects related to (1) tooth structures, (2) periodontal tissues, (3) undesired treatment results, (4) relapse and stability, and (5) negative qualitative experiences by the patient or carer(s) (Table 7). These were also the most prevalent types of adverse effects sought in the included studies and reported in the review and accounted for 83.1% (162/195) of all adverse effects sought and reported (Table 8). We were able to categorize all 195 adverse effects except one and labeled it 'Additional adverse effects' (Table 8).

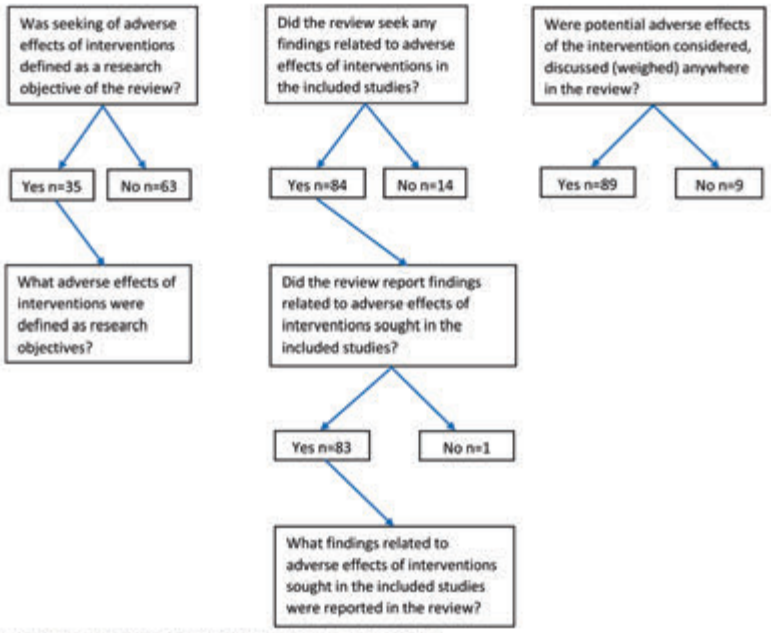


**Fig. 3** Seeking adverse effects in systematic reviews of orthodontic interventions

**Table 4** Outcomes on seeking adverse effects in systematic reviews of orthodontic interventions

| Description of outcomes | Cochrane | EJO | AJODO | AO | KJO | O&CR | All orthodontic journals | All journals |
|---|---|---|---|---|---|---|---|---|
| The number of identified systematic reviews | 29 | 100 | 68 | 61 | 11 | 53 | 293 | 322 |
| The number of eligible systematic reviews of orthodontic interventions | 10 | 28 | 20 | 23 | 3 | 14 | 88 | 98 |
| The prevalence of eligible systematic reviews of orthodontic interventions that defined seeking of adverse effects of interventions as a research objective of the review[a] | 20.0% (2/10) | 32.1% (9/28) | 45% (9/20) | 21.7 (5/23) | 33.3% (1/3) | 64.3% (9/14) | 47.7% (33/88) | 35.7% (35/98) |
| The prevalence of eligible systematic reviews of orthodontic interventions that sought any findings related to adverse effects of interventions in the included studies[a] | 100.0% (10/10) | 92.9% (26/28) | 75.0% (15/20) | 78.3% (18/23) | 100.0% (3/3) | 85.7% (12/14) | 84.1% (74/88) | 85.7% (84/98) |
| The prevalence of eligible systematic reviews of orthodontic interventions that reported findings related to the adverse effects of interventions sought in the included studies[a] | 100.0% (10/10) | 92.9% (26/28) | 70.0% (14/20) | 78.3% (18/23) | 100.0% (3/3) | 85.7% (12/14) | 83.0% (73/88) | 84.7% (83/98) |
| The prevalence of eligible systematic reviews of orthodontic interventions that considered, discussed (weighed) potential adverse effects of the intervention anywhere in the review [a] | 100.0% (10/10) | 92.9% (26/28) | 85.0% (17/20) | 91.3% (21/23) | 100.0% (3/3) | 85.7% (12/14) | 89.8% (79/88) | 90.8% (89/98) |

[a] The denominator for calculating the proportions for each journal is the number of included reviews for that journal. The denominator for calculating the proportions for all journals together is the total of included reviews, i.e., 98

**Table 5** Outcomes on seeking adverse effects in systematic reviews of orthodontic interventions by year of publication

| | | Was seeking of adverse effects of interventions defined as a research objective of the review | | Did the review seek any findings related to adverse effects of interventions in the included studies? | | Did the review report findings related to adverse effects of interventions sought in the included studies? | | Were potential adverse effects of the intervention considered, discussed (weighed) anywhere in the review? | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Year | | Yes | No | Yes | No | Yes | No | Yes | No | Total |
| 2009 | Count | 0 | 1 | 1 | 0 | 1 | 0 | 1 | 0 | 1 |
| | % within Year | 0.0% | 100.0% | 100.0% | 0.0% | 100.0% | 0.0% | 100.0% | 0.0% | 100.0% |
| 2010 | Count | 1 | 2 | 2 | 1 | 2 | 1 | 3 | 0 | 3 |
| | % within Year | 33.3% | 66.7% | 66.7% | 33.3% | 66.7% | 33.3% | 100.0% | 0.0% | 100.0% |
| 2011 | Count | 3 | 4 | 6 | 1 | 6 | 1 | 6 | 1 | 7 |
| | % within Year | 42.9% | 57.1% | 85.7% | 14.3% | 85.7% | 14.3% | 85.7% | 14.3% | 100.0% |
| 2012 | Count | 2 | 0 | 2 | 0 | 2 | 0 | 2 | 0 | 2 |
| | % within Year | 100.0% | 0.0% | 100.0% | 0.0% | 100.0% | 0.0% | 100.0% | 0.0% | 100.0% |
| 2013 | Count | 3 | 6 | 9 | 0 | 9 | 0 | 9 | 0 | 9 |
| | % within Year | 33.3% | 66.7% | 100.0% | 0.0% | 100.0% | 0.0% | 100.0% | 0.0% | 100.0% |
| 2014 | Count | 3 | 6 | 7 | 2 | 7 | 2 | 7 | 2 | 9 |
| | % within Year | 33.3% | 66.7% | 77.8% | 22.2% | 77.8% | 22.2% | 77.8% | 22.2% | 100.0% |
| 2015 | Count | 3 | 9 | 9 | 3 | 9 | 3 | 12 | 0 | 12 |
| | % within Year | 25.0% | 75.0% | 75.0% | 25.0% | 75.0% | 25.0% | 100.0% | 0.0% | 100.0% |
| 2016 | Count | 1 | 8 | 6 | 3 | 6 | 3 | 7 | 2 | 9 |
| | % within Year | 11.1% | 88.9% | 66.7% | 33.3% | 66.7% | 33.3% | 77.8% | 22.2% | 100.0% |
| 2017 | Count | 2 | 7 | 8 | 1 | 7 | 2 | 8 | 1 | 9 |
| | % within Year | 22.2% | 77.8% | 88.9% | 11.1% | 77.8% | 22.2% | 88.9% | 11.1% | 100.0% |
| 2018 | Count | 4 | 9 | 10 | 3 | 10 | 3 | 10 | 3 | 13 |
| | % within Year | 30.8% | 69.2% | 76.9% | 23.1% | 76.9% | 23.1% | 76.9% | 23.1% | 100.0% |
| 2019 | Count | 3 | 1 | 4 | 0 | 4 | 0 | 4 | 0 | 4 |
| | % within Year | 75.0% | 25.0% | 100.0% | 0.0% | 100.0% | 0.0% | 100.0% | 0.0% | 100.0% |
| 2020 | Count | 7 | 5 | 12 | 0 | 12 | 0 | 12 | 0 | 12 |
| | % within Year | 58.3% | 41.7% | 100.0% | 0.0% | 100.0% | 0.0% | 100.0% | 0.0% | 100.0% |
| 2021 | Count | 3 | 5 | 8 | 0 | 8 | 0 | 8 | 0 | 8 |
| | % within Year | 37.5% | 62.5% | 100.0% | 0.0% | 100.0% | 0.0% | 100.0% | 0.0% | 100.0% |
| Total | Count | 35 | 63 | 84 | 14 | 83 | 15 | 89 | 9 | 98 |
| | % within Year | 35.7% | 64.3% | 85.7% | 14.3% | 84.7% | 15.3% | 90.8% | 9.2% | 100.0% |

**Table 6** Results of univariable logistic regression including journal as a predictor variable of seeking adverse effects as an objective of the systematic review

| Journal | Odds ratio | Lower 95% CI | Upper 95% CI | *P* value |
|---|---|---|---|---|
| Cochrane | 1 | – | – | – |
| AJODO | 3.27 | 0.55 | 19.45 | 0.19 |
| AO | 1.11 | 0.18 | 6.99 | 0.91 |
| EJO | 1.90 | 0.33 | 10.80 | 0.47 |
| KJO | 2.00 | 0.12 | 34.82 | 0.63 |
| O&C | 7.20 | 1.08 | 47.96 | 0.04 |

**Table 7** Type of adverse effects defined as research objectives of the review

| Adverse effects related to | Prevalence |
|---|---|
| Tooth structures | 16.7% (8/48) |
| Periodontal tissues | 12.5% (6/48) |
| Intraoral (non-tooth or periodontal) tissues | 0.0% (0/48) |
| Extraoral tissues (non-temporomandibular tissues) | 0.0% (0/48) |
| Temporomandibular tissues and disorders | 2.1% (1/48) |
| Undesired treatment results | 18.8% (9/48) |
| Relapse and stability | 20.8% (10/48) |
| Negative qualitative experiences by the patient or carer(s) | 18.8% (9/48) |
| Appliance failure | 0.0% (0/48) |
| Gastro-intestinal | 0.0% (0/48) |
| Non-defined | 10.4% (5/48) |
| Additional adverse effects | 0.0% (0/48) |

**Table 8** Type of adverse effects sought and reported in the review

| Adverse effects related to | Prevalence |
|---|---|
| Tooth structures | 12.8% (25/195) |
| Periodontal tissues | 13.8% (27/195) |
| Intraoral (non-tooth or periodontal) tissues | 2.6% (5/195) |
| Extraoral tissues (non-temporomandibular tissues) | 0.5%(1/195) |
| Temporomandibular tissues and disorders | 4.1% (8/195) |
| Undesired treatment results | 22.1% (43/195) |
| Relapse and stability | 18.5% (36/195) |
| Negative qualitative experiences by the patient or carer(s) | 15.9% (31/195) |
| Appliance failure | 7.7% (15/195) |
| Gastro-intestinal | 0.5%(1/195) |
| Non-defined | 1.0% (2/195) |
| Additional adverse effects[a] | 0.5%(1/195) |

[a] General disorders, injury, poisoning and procedural complications, musculoskeletal and connective tissue disorders, nervous system disorders and respiratory, thoracic and mediastinal disorders, safety of the adjunctive intervention



## Discussion

### Principal findings of the study

This cross-sectional study showed that in 35.7% (35/98) of reviews of orthodontic interventions seeking of adverse effects was defined as an objective. In 85.7% (84/98) of these reviews, findings related to adverse effects of interventions were sought and in 84.7% (83/98) the reviewers reported on these findings. In more than 90% (89/98) of included systematic reviews, the reviewers discussed (weighed) potential adverse effects of interventions somewhere in the review. Five types of adverse effects accounted for 83.1% (162/195) of adverse effects that were sought and reported in the eligible reviews.

### Comparisons with other studies

The proportion of included reviews that defined seeking of adverse effects as a research objective was low, i.e., 35.7% (35/98) in both Cochrane and non-Cochrane systematic reviews (Table 4). Assessing potential adverse effects of interventions is considered a mandatory item when setting the research question for Cochrane intervention reviews [1]. Not defining seeking of adverse effects as a research objective can mislead end-users of systematic reviews. Authors therefore need to include this item in their research objectives and editors and peer reviewers should verify its implementation.

The proportions of reviews that reported findings related to adverse effects of interventions were higher in this sample of orthodontic reviews (84.7%(83/98) compared with gastroenterology reviews (66.7% (52/78) [18], Cochrane reviews of interventions (75.6% (59/78), and Database of Abstracts of Reviews of Effects (DAREs) reviews (48.1% (38/79) [38]. Explanations for these higher proportions could be: (1) the time period of inclusion of reviews (2) the research design and type of interventions of the studies included in the reviews (3) the field of research. Orthodontic research could be more focused on assessing adverse effects of interventions than other fields, because this assessment is an integral part of routine clinical practice. For example, assessing adverse effects such as undesired

treatment results and relapse and stability are part of everyday problems in orthodontic practice and accounted for 40.5% (79/195) of adverse effects sought and reported in this sample of systematic reviews of orthodontic interventions (Table 8).

***Strengths and limitations***

This cross-sectional study has the following strengths: (1) scoping searches were conducted to identify knowledge gaps, (2) pilot studies were conducted to calibrate researchers and fine-tune research questions and methodology, (3) a protocol was developed and published a priori [6], and (4) all raw data were included with this manuscript or recorded in Open Science Framework (https://osf.io/ka7mp/). This study also has limitations. First, the findings of this cross-sectional study are expected to be better than those reported in the entire body of orthodontic literature, because we assessed reviews published in the five leading orthodontic journals and those listed in the Cochrane Database of Systematic Reviews. Second, the risk of selective (non) reporting bias regarding adverse effects in the eligible reviews. Third, only reviews published in a pre-established period (August 1 2009 until July 31 2021) were eligible, instead of having considered a larger sample, e.g., by having included reviews prior to the inception date. However, we chose this inception date, because it coincides with the launch of the PRISMA statement [31, 32], which provides reviewers better guidance on reporting.

***Implications and future research***

Several of our findings seem promising at a first glance. For example, the proportion of reviews that sought and reported adverse effects was relatively high, i.e., (84.7% (83/98), but a variety of issues has to be considered when interpreting this finding. First, this proportion only refers to whether or not reviewers implemented this item, but not how. For example, the reviewers could have reported on just one or a selection of all adverse effects assessed and reported in the eligible studies for their reviews. Second, this proportion also does not give any information on the magnitude, and duration of adverse effects nor on the time points for assessing them. Third, we do not know whether all adverse effects were indeed sought and reported as originally planned in the registered protocols of the included reviews. For example, Parsons et al. [39] showed that this was not the case in their sample of systematic reviews of health care interventions. In 35% (51/146) of these reviews they found discrepancies between what was planned in the protocol as registered in PROSPERO and what was reported on adverse effects in the final published reviews. Fourth, a wide body of evidence has shown that adverse events were often assessed inconsistently and reported inadequately in clinical trials and that most results on these events were not available in public sources [8, 40–42]. If these limitations also apply to the clinical trials that fed the reviews of this study one should further question the validity of the findings on adverse effect of systematic reviews of orthodontic interventions.

Strategies to improve the validity of what is reported on adverse effects of orthodontic interventions in systematic reviews include developing tailored core outcome sets on these effects [43] as well as guidelines for assessing and reporting them in both primary research and systematic reviews. Additional strategies on synthesizing adverse effects in systematic reviews at multiple levels were published in a recent paper by Qureshi et al. [19]. By

implementing such strategies progress on the assessing and reporting of adverse effects of orthodontic interventions in both primary studies and systematic reviews can be made.

In conclusion the promising findings of this study should be interpreted with caution by its end users, because they could be jeopardized by numerous uncertainties. Much research is ahead to create valid and usable knowledge on adverse effects of orthodontic interventions involving a wide body of stakeholders.



**Abbreviations**

AJODO American Journal of Orthodontics and Dentofacial Orthopedics
AO Angle Orthodontist
CONSORT Consolidated Standards of Reporting Trials
EJO European Journal of Orthodontics
KJO Korean Journal of Orthodontics
O&CR Orthodontics and Craniofacial Research
PRISMA Preferred reporting items for systematic reviews and meta-analyses
PROSPERO Prospective Register of Systematic Reviews
STROBE Strengthening the Reporting of Observational Studies in Epidemiology

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13643-023-02273-7.

**Additional file 1.** STROBE Statement: Checklist of items that should be included in reports of cross-sectional studies [25].

**Additional file 2.** A. Differences between the protocol and the completed cross-sectional study. B. Selected journals and their 2018 impact factor (Clarivate Analytics 2021). C. Data collection forms*. D. Adverse effects hypothetically linked to orthodontic interventions according to Preoteasa et al. [24]*. E. Adverse effects hypothetically linked to orthodontic interventions*.

**Additional file 3.** Included reviews.

**Additional file 4.** Excluded studies.

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**Authors' contributions**
PS and RMR conceived and designed this cross-sectional study and RMR is the guarantor. PS and RMR conducted the study selection procedures and data extraction. PS, RMR, and NDG conducted the data analyses and statistical analyses. SB provided support on methodological

issues and assisted in the overall fine-tuning of this cross-sectional study. All four authors revised the various draft versions of this paper and read and approved the final submitted manuscript.

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**Competing interests**
Reint Meursinge Reynders and Shandra Bipat are both Associate Editors for Systematic Reviews. All four authors declare that they have no further competing interests.

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**Publisher's Note**

# CHAPTER 4

## Spin in the reporting, interpretation, and extrapolation of adverse effects of orthodontic interventions: protocol for a cross-sectional study of systematic reviews

This is a non-edited version of the manuscript:

Steegmans PAJ, Di Girolamo N, Meursinge Reynders RA. Spin in the reporting, interpretation, and extrapolation of adverse effects of orthodontic interventions: protocol for a cross- sectional study of systematic reviews. Res Integr Peer Rev. 2019 Dec 19;4:27.

## Abstract

**Background**: Titles and abstracts are the most read sections of biomedical papers. It is therefore important that abstracts transparently report both the beneficial and adverse effects of health care interventions and do not mislead the reader. Misleading reporting, interpretation, or extrapolation of study results is called “spin”. In this study, we will assess whether adverse effects of orthodontic interventions were reported or considered in the abstracts of both Cochrane and non-Cochrane reviews and whether spin was identified and what type of spin.

**Methods:** Eligibility criteria were defined for the type of study designs, participants, interventions, outcomes, and settings. We will include systematic reviews of clinical orthodontic interventions published in the five leading orthodontic journals and in the Cochrane Database. Empty reviews will be excluded. We will manually search eligible reviews published between 1 August 2009 and 31 July 2019. Data collection forms were developed a priori. All study selection and data extraction procedures will be conducted by two reviewers independently. Our main outcomes will be the prevalence of reported or considered adverse effects of orthodontic interventions in the abstract of systematic reviews and the prevalence of “spin” related to these adverse effects. We will also record the prevalence of three subtypes of spin, i.e., misleading reporting, misleading interpretation, and misleading extrapolation- related spin. All statistics will be calculated for the following groups: (1) all journals individually, (2) all journals together, and (3) the five leading orthodontic journals and the Cochrane Database of Systematic Reviews separately. Generalized linear models will be developed to compare the various groups.

**Discussion:** We expect that our results will raise the awareness of the importance of reporting and considering of adverse effects and the presence of the phenomenon of spin related to these effects in abstracts of systematic reviews of orthodontic interventions. This is important, because an incomplete and inadequate reporting, interpretation, or extrapolation of findings on adverse effects in abstracts of systematic reviews can mislead readers and could lead to inadequate clinical practice. Our findings could result in policy implications for making judgments about the acceptance for publication of systematic reviews of orthodontic interventions.

**Keywords:** Orthodontics, Reporting, Systematic review, Intervention, Spin, Misleading reporting, Misleading interpretation, Misleading extrapolation, Adverse effect, Adverse event, Harm, Safety

## Background

Readers of the biomedical literature mostly just screen the title and the abstract of an article without assessing the full publication [1]. The beneficial and adverse effects of interventions should therefore be transparently reported in these summaries and should not mislead its readers. Misleading reporting, interpretation, or extrapolation of study results is called "spin" [2–4]. We will assess in abstracts of both Cochrane and non-Cochrane reviews whether adverse effects of orthodontic interventions were reported or considered and whether spin was identified and what type of spin.

Titles and abstracts are the most read sections of biomedical papers [1], because assessing the full research article is often conditioned by paywalls or because of a lack of time or language issues of the readers [1]. Abstracts should therefore clearly and truthfully reflect the objectives, methods, results, and the interpretation of research findings. The standard for Methodological Expectations of Cochrane Intervention Reviews (MECIR) [5] has listed a series of highly desirable and mandatory items that should be consulted by reviewers when preparing the abstract of their reviews. Item R13 of the MECIR standard states that: "The Abstract of the review should aim to reflect a balanced summary of the benefits and harms of the intervention." This mandatory item is particularly crucial for presenting adverse effects of health care interventions, because these effects are often poorly reported in systematic reviews [6]. Numerous epidemiological studies have also shown that the assessment and reporting of adverse effects of interventions in primary research studies is often suboptimal [7–11]. We adopted Cochrane's definition of adverse effects: "An adverse event for which the causal relation between the intervention and the event is at least a reasonable possibility" [12, 13]. This definition and other key terminology in this manuscript are summarized in Table 1 [2– 4, 12–15].

When presenting information on adverse effects in the abstract, it is also crucial that it does not mislead the reader. A distorted presentation of study results has been defined as "spin" [3], but more elaborate definitions are also used (Table 1). The term spin was first used in 1995 in the medical literature by Horton [16] and has been further subdivided into three categories [4]: misleading reporting-related spin, misleading interpretation-related spin, and misleading extrapolation-related spin (Table 1). Yavchitz et al. [17] have ranked the various types of spin according to their severity. The severest form of spin in abstracts of systematic reviews and meta-analyses was scored for "conclusions that contain recommendations for clinical practices that were not supported by findings" [17]. A high prevalence of the various types of spin has been identified in multiple epidemiological studies [4, 18– 22]. Boutron et al. [18] found spin in 50% (36/72) of the conclusions sections of the main text of parallel-group RCTs and in 58.3% (42/72) of the conclusions sections of the abstracts. Spin was also common in diagnostic accuracy studies published in journals with high impact factors [22]. Lockyer et al. [21] showed that spin is a frequent phenomenon in abstracts of RCTs of wound treatments, and Lazarus et al. [4] identified at least one example of spin in 84% (107/128) of the abstracts of non-randomized intervention studies. Spin is in strong conflict with the Declaration of Helsinki [23] that states that: "Authors have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports."

In this study, we will assess whether potential adverse effects of orthodontic interventions were reported or considered (i.e., discussed, weighed, etc.) in the abstract of systematic reviews. We will further assess whether spin was introduced regarding information on these adverse effects in the abstract, and we will categorize the types of spin (Table 1). We will assess these issues in the five leading orthodontic journals and those included in the Cochrane Database of Systematic Reviews. In these reviews, we will assess adverse effects such as pain as a result of tooth movement and the adverse effects defined by Preoteasa et al. (Table 2) [24]. Scoping searches in the orthodontic literature confirmed the knowledge gaps on our research questions. Our pilot studies quantified these gaps and confirmed the need to address these questions. We will assess these issues in systematic reviews, because they are increasingly consulted by patients [25] and when well-conducted systematic reviews are considered among the information sources with the highest level of evidence [26]. Our research questions are important, because incomplete or misleading information on adverse effects of interventions may have detrimental effects on the treatment of orthodontic patients.

**Table 1** Glossary of terms

| Term | Definition |
|---|---|
| Systematic review | The Cochrane glossary [12] defines a systematic review as "A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies." |
| Intervention review | Cochrane [14] defines an intervention review as follows: "Intervention reviews assess the benefits and harms of interventions used in healthcare and health policy." |
| Orthodontic interventions | Steegmans et al. [15] define orthodontic interventions as follows: "Orthodontic interventions refer to the use of any type of orthodontic appliance that are used to move teeth or change the jaw size or position for orthodontic purposes. These interventions also include appliances to maintain or stabilize the results of orthodontic treatment, for example retainers." |
| Adverse effect | Cochrane [12, 13] defines an adverse effect as "an adverse event for which the causal relation between the intervention and the event is at least a reasonable possibility." |
| Spin [3] | "Distorted presentation of study results." |
| Spin [3] | "A misrepresentation of study results, regardless of motive (intentionally or unintentionally) that overemphasizes the beneficial effects of the intervention and overstates safety compared with that shown by the results." |
| Spin [2] | "A specific intentional or unintentional reporting that fails to faithfully reflect the nature and range of findings and that could affect the impression the results produce in readers." |
| Misleading reporting related-spin [4] | "Incomplete reporting of the study results that could be misleading for the reader." |
| Misleading interpretation related-spin [4] | Inadequate interpretation of the study results overestimating the beneficial effect of the intervention. |
| Misleading extrapolation related-spin [4] | Inappropriate generalization of the study results by inadequate (1) extrapolation from the population, interventions, or outcome actually assessed in the study to a larger population, different interventions, or outcomes, or (2) inadequate implications for clinical practice. |
| Spin (in the abstract) on adverse effects of interventions | Incomplete or inadequate reporting, interpretation, or extrapolation (or a combination of these variables) of findings on adverse effects of interventions in the abstract that could be misleading for the reader. |

**Table 2** Adverse effects hypothetically linked to orthodontic interventions [24]

| Subgroup | Description |
|---|---|
| Local adverse effects | |
| Dental | • Crown: decalcifications, decays, tooth wear, enamel cracks and fractures; discolorations, deterioration of prosthetic crown (as fracturing a ceramic one during debonding); |
| | • Root: root resorption, early closure of root apex, ankylosis; |
| | • Pulp: ischemia, pulpitis, necrosis; |
| Periodontal | • Gingivitis, periodontitis, gingival recession or hypertrophy, alveolar bone loss, dehiscences, fenestrations, interdental fold, dark triangles; |
| Temporomandibular joint | • Condylar resorption, temporomandibular dysfunction; |
| Soft tissues of the oral and maxillofacial region | • Trauma (e.g., long archwires, headgear related), mucosal ulcerations or hyperplasia, chemical burns (e.g., etching related), thermal injuries (e.g., overheated burs), stomatitis, clumsy handling of dental instruments; |
| Unsatisfactory treatment outcome | • Inadequate morpho-functional, aesthetic or functional final result, relapse, failure to complete treatment due to treatment dropout. |
| Systemic adverse effects | |
| Psychological | • Teasing, behavioral changes of patients and parents; discomfort associated with pain presence and aesthetic look discontents during orthodontic appliance usage; |
| Gastro-intestinal | • Accidental swallowing of small parts of the orthodontic device (tubes, brackets); |
| Allergies | • To nickel or latex; |
| Cardiac | • Infective endocarditis; |
| Chronic fatigue syndrome | |
| Cross infections | • From doctor to patient, patient to doctor, patient to patient. |





## Objectives

The objectives of this research study are summarized in the following research questions:

Research questions

- In abstracts of systematic reviews of orthodontic interventions, were potential adverse effects of these interventions reported or considered (i.e., discussed, weighed, etc.)?
- In abstracts of systematic reviews of orthodontic interventions, was spin identified in the reporting, interpretation, and extrapolation of adverse effects?
- What was the prevalence of each type of spin?

## Methods

This protocol is reported according to the guidance of the Preferred Reporting Items for Systematic Review and Meta- Analysis Protocols (PRISMA-P) 2015 statement, and the PRISMA-P checklist is included as Additional file 1 [27, 28]. We adopted the same flow of research methods as reported in our published protocol on seeking adverse effects in systematic reviews of orthodontic interventions (Fig. 1) and con- ducted our pilot tests on the same sample of systematic reviews as was described in our previous protocol [15]. Our sample size of 14 reviews for the pilot test was calculated with the formula reported by Viechtbauer et al. [29]. Further details on the methods of our pilot test are reported in Additional file 2. This pilot test found that the reviewers in only 35.7% (5/14) of the abstracts reported or considered (i.e., dis- cussed, weighed) potential adverse effects of orthodontic interventions. This sample identified an overall prevalence of 14.3% (2/14) of spin in the abstract on adverse effects of orthodontic interventions. Both cases of spin were "misleading reporting-related spin." The following sections describe our planned methods based on these pilot tests. We will not start the selection of eligible reviews and data extraction prior to the complete acceptance of this protocol for publication.

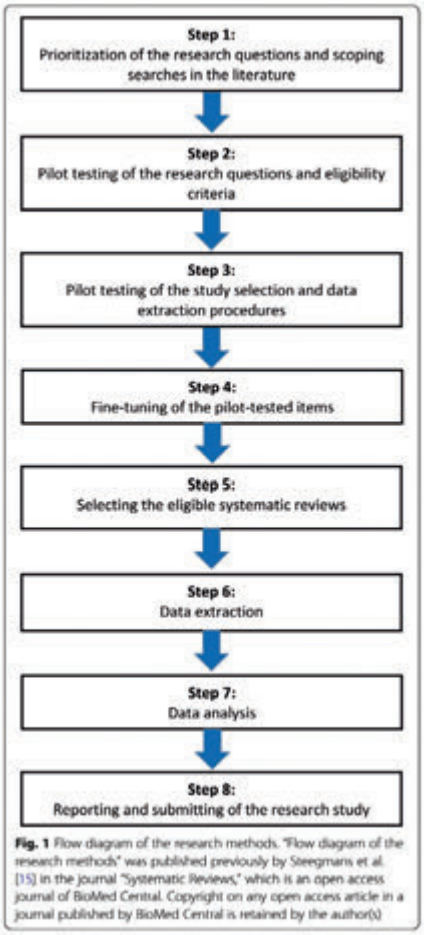


**Fig. 1** Flow diagram of the research methods. "Flow diagram of the research methods" was published previously by Steegmans et al. [15] in the journal "Systematic Reviews," which is an open access journal of BioMed Central. Copyright on any open access article in a journal published by BioMed Central is retained by the author(s)

### Eligibility criteria

We will adopt the same eligibility criteria that were defined for our published protocol on seeking adverse effects in systematic reviews of orthodontic interventions [15]. To avoid misinterpretation, we copied and pasted these eligibility criteria into Table 3 [15, 30].

### Information sources

We will manually search the Cochrane library [14] and the websites of the five leading orthodontic journals to identify eligible systematic reviews published between 1 August 2009 and 31 July 2019. We chose this starting date because the first of August 2009 coincides with the launch of the Preferred Reporting Items for Systematic Reviews and

Meta-Analyses (PRISMA) statement and its guidance paper on 21 July 2009 [27, 28]. Journal selection was based on two criteria: (1) the journal has been published for 10 years or more and (2) the impact factor. The journal citation reports by Clarivate Analytics were consulted to identify the five leading orthodontic journals based on impact factor [31]. The following five orthodontic journals fulfilled both criteria: European Journal of Orthodontics (EJO), American Journal of Orthodontics and Dentofacial Orthopedics (AJODO), Angle Orthodontist, The Korean Journal of Orthodontics, and Orthodontics and Craniofacial Research.

**Table 3** Eligibility criteria

| Item | Included | Excluded |
|---|---|---|
| Study designs | Systematic reviews of orthodontic interventions. The definition of systematic review, intervention review, and orthodontic interventions listed in the Glossary of terms will be used to assess whether a review is eligible (Table 1). | (1) Non-interventional reviews such as, "Methodology," "Diagnostic," "Qualitative," and "Prognostic"<br>(2) Rapid and scoping reviews<br>(3) Systematic reviews that focus exclusively on adverse effects of interventions<br>(5) Systematic reviews of interventions that did not find any eligible studies (empty reviews) |
| Participants | Systematic reviews on any type of patients undergoing orthodontic interventions, i.e., patients of any health status, sex, age, demographics, and socio-economic status. | (1) Intervention reviews that focus exclusively on patients with congenital anomalies, for example with cleft lip and palate<br>(2) Systematic reviews of animal or laboratory studies |
| Interventions | (1) Systematic reviews that assess the effects of clinical orthodontic interventions. Clinical orthodontic interventions refer to the use of any type of orthodontic appliance that is used to move teeth or change the jaw size or position for orthodontic purposes<br>(2) Systematic reviews of interventions with appliances to maintain or stabilize the outcomes of orthodontic treatment, for example, retainers<br>(3) Systematic reviews of orthodontic interventions that compare the effects of orthodontic treatment with or without additional interventions such as pharmacological or small surgical interventions, e.g., periodontal or implant surgery<br>(4) No exclusion criteria will be applied to the characteristics of the operator who conducted the interventions | (1) Systematic reviews in which patients receive orthodontic treatment, but in which the effects of other interventions, e.g., periodontal surgery, are compared and not the effects of orthodontic interventions<br>(2) Systematic reviews of interventions in which orthodontic appliances are specifically used for other purposes, e.g., changing jaw positions to treat respiration or temporomandibular disorders<br>(3) Systematic review of orthodontic interventions that included orthognathic surgery |
| Outcomes | (1) Any adverse effect of orthodontic interventions scored at any endpoint or timing<br>(2) The effects of orthodontic interventions do not refer just to outcomes related to tooth and jaw size and positions, but also to broader outcomes such as periodontal health, esthetic changes, the health of the temporomandibular joint, patient health experiences, and economic issues associated with the interventions<br>(3) The reporting of outcomes on adverse effects will not determine the eligibility of reviews for this cross-sectional study, i.e., reviews will not be excluded because they did not provide "usable" data [30] | No exclusion criteria |
| Stetting | Any type of setting in which the interventions were conducted, i.e., university or private practice, etc. | No exclusion criteria |

**Study records**

***Data management***

- Two authors (PS and RMR) will conduct all study selection and data extraction procedures independently.
- Pilot tests were conducted to train both reviewers in applying these methods consistently and for calibration purposes [28].
- We will apply the following strategies in the case of disagreement between the two authors on the eligibility of a paper or the extraction of data: (1) discussions between

reviewers, (2) rereading the paper, (3) or if necessary contacting its authors [32]. Persistent disagreements will be resolved through the consultation and arbitration of a methodologist (NDG).
- All eligible systematic reviews will be downloaded, and all extracted data will be collected in an Excel spreadsheet.

***Selection process***

- All titles and abstracts in the websites of the five orthodontic journals will be hand-searched to identify eligible reviews. The section "Dentistry and Oral health" will be searched in the Cochrane library for eligible Cochrane reviews [14].
- We will only include the latest version of a review when updates have been published.
- Authors will be contacted in the case of doubt regarding multiple publications of the same review. We plan to include the first publication, but will make this decision on a case by case basis and will report the rationale for this choice.
- Our selection procedures will be presented in a PRISMA flow diagram [32, 33].
- All included and excluded studies will be presented in tables, and the rationale for exclusion will be given for each excluded review.

***Data collection process***

- All eligible studies together with their supplemental files will be merged into binder PDFs, and pertinent search terms are linked to these documents to facilitate data extraction [34, 35].
- Eligible search terms were identified through searches in thesauri and in key articles on adverse effects [13, 36–40]. These terms are given in Additional file 3 and are identical to those used in our protocol on seeking adverse effects in systematic reviews of orthodontic interventions [15].
- Our pilot-tested data collection forms will be used for all data extraction procedures (Additional file 4). The PRISMA [32, 33] and the PRISMA-P [27, 28] checklists and guidance were consulted to develop these forms. The criteria for scoring pertinent data items are defined in these forms.
- The entire eligible review of both orthodontic and Cochrane reviews will be searched for data items, i.e., the text, tables, figures, and all supplemental files. The plain language summary in the eligible Cochrane reviews will not be searched for data items.
- When during the data extraction procedure changes are made in the data collection forms, we will present this with rationale in the section "Differences between the protocol and review."

***Scoring adverse effects of orthodontic interventions***

- We will use the framework of categories of known orthodontic adverse effects as defined by Preoteasa et al. [24] (Table 2). We will also include pain as a result of tooth movement as an adverse effect. Potential adverse effects that are identified

during data extraction will be discussed between the two reviewers (PS and RMR). We will report the rationale when including additional adverse effects and will categorize them.

- Ambiguous outcomes that could be interpreted as either a beneficial or an adverse outcome will not be scored as "adverse." The rationale for this score will be given. We will only consider ambiguous outcomes as "adverse" when the review authors define these outcomes as such and make a strong case for this classification.

***Scoring spin in the reporting, interpretation, and extrapolation of adverse effects of orthodontic interventions***

- We will assess three types of spin, i.e., misleading reporting, misleading interpretation, and misleading extrapolation on adverse effects of orthodontic interventions in the abstract (Table 4). Each type of spin will be assessed separately for reviews that either did or did not seek adverse effects of interventions.
- To facilitate our scoring procedures and to reduce the risk of misinterpretation, we subdivided each type of spin into categories and defined each category (Table 4). We will score the presence of spin when spin is identified for one or more of these categories. The scoring procedures are summarized in Additional file 4. Pilot tests were conducted to assess the validity of these procedures.

**Table 4** Types of spin in reviews that did or did not seek adverse effects of interventions

| Definitions of the three types of spin | Reviews that sought adverse effects of interventions | Reviews that did not seek adverse effects of interventions |
|---|---|---|
| Misleading reporting (in the abstract) on adverse effects of interventions:<br>"Incomplete or inadequate reporting in the abstract on the results of adverse effects compared with what is reported in the main text of the manuscript, which could be misleading for the reader." | Categories:<br>(1) Not reporting in the abstract on the results of the adverse effects that were reported in the main text of the review.<br>(2) Selective reporting in the abstract on the results of the adverse effects that were reported in the main text of the review. | Categories:<br>(1) Reporting on results of adverse effects in the abstract when adverse effects were not sought.<br>(2) Reporting in the abstract that adverse effects were sought when they were not sought. |
| Misleading interpretation (in the abstract) on adverse effects of interventions:<br>"Interpretation in the abstract on the results of adverse effects that is not consistent with what is reported in the main text of the manuscript and underestimates the adverse effects of the intervention." | Categories:<br>(1) Claiming in the abstract that the intervention is safe (has no or minimal adverse effects), despite concerning results on the adverse effects in the main text of the review, e.g., based on non-statistically significant results on adverse effects with wide confidence intervals [17].<br>(2) Downgrading in the abstract the importance of the adverse effects, despite concerning results on the adverse effects in the main text of the review.<br>(3) Recommendations are made in the abstract for clinical practice that are not congruent with the concerning results on the adverse effects in the main text of the review [17]. | Categories:<br>(1) Claiming in the abstract that the intervention is safe (has no or minimal adverse effects) despite not having sought adverse effects.<br>(2) Downgrading in the abstract the importance of the adverse effects, despite not having sought adverse effects.<br>(3) Recommendations are made in the abstract for clinical practice despite not having sought adverse effects. |
| Misleading extrapolation (in the abstract) on adverse effects of interventions:<br>"Overgeneralisation in the abstract of the study results to different populations, interventions, outcomes or settings than were assessed in the study despite evidence in the main text on concerning adverse effects on a different population, intervention, outcome or setting." | Categories:<br>(1) Results are extrapolated in the abstract to another population, intervention, outcome, or setting than were assessed in the review despite evidence in the main text on concerning adverse effects on a different population, intervention, outcome or setting. | Categories:<br>(1) Results are extrapolated in the abstract to another population, intervention, outcome, or setting than were assessed in the review despite not having sought adverse effects. |

**Outcomes and statistical analyses**

- Figure 2 a and b present all research questions in a flow diagram, and Table 5 lists all planned outcomes.
- We will calculate and report all prevalence data with their 95% confidence levels.
- We calculate the prevalence statistics for (1) all journals as one group, (2) the group of five leading orthodontic journals and the Cochrane Database of Systematic Reviews separately, and (3) each individual journal separately. Generalized linear models will be developed having the following outcomes for the abstracts of systematic reviews of orthodontic interventions: the reporting or considering of potential adverse effects of interventions/no reporting or considering of potential adverse effects of interventions (binary); presence of SPIN/absence of "SPIN" (binary); and misleading reporting/misleading interpretation/misleading extrapolation/no SPIN (categorical). The models will account for journal category (Cochrane Database of Systematic Reviews vs others), individual journals, and the geographical location of the study. Statistical significance will be based on a p value < 0.05. Stata software (Stata Corporation, College Station, TX, USA) version 15 will be used for all the statistical analyses [41].
- All outcomes that will be introduced or eliminated post hoc will be reported together with the rationale for inclusion or exclusion.

**Reporting of the research study and data management**

- The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement will be used as the guideline for reporting the completed cross-sectional study [42].
- A data management plan was prepared for the long-term storage of our research data [43] in the case that the publisher of our completed research study will not or will only partly store our raw data. We consulted the Registry of Research Data Repositories [44] to identify an appropriate repository for our type of research data. We selected Dryad [45] for two reasons: (1) it is an international repository of data of peer-reviewed scientific and medical research and (2) it also includes data sets for which no specific data repository exist such as meta- epidemiological research data of systematic reviews in orthodontics. Our data management plan implies that (1) all our research data will be made freely available, (2) our completed article will present a link to a repository in which all raw data of the study will be deposited, (3) the repository is registered in the Registry of Research Data Repositories [44], (4) our research data will be reported in a format that permits other researchers to understand, cite, and reuse these data, (5) all sensitive data will be protected, and (6) it will be reassessed frequently and also updated if necessary [43, 44].

**Differences between the protocol and the completed study**

- We will report all modifications between the protocol and the final research study. The rationale for each of these changes will be given.
- We will also report the consequences of these modifications on the magnitude, direction, and the validity of the outcomes [46].

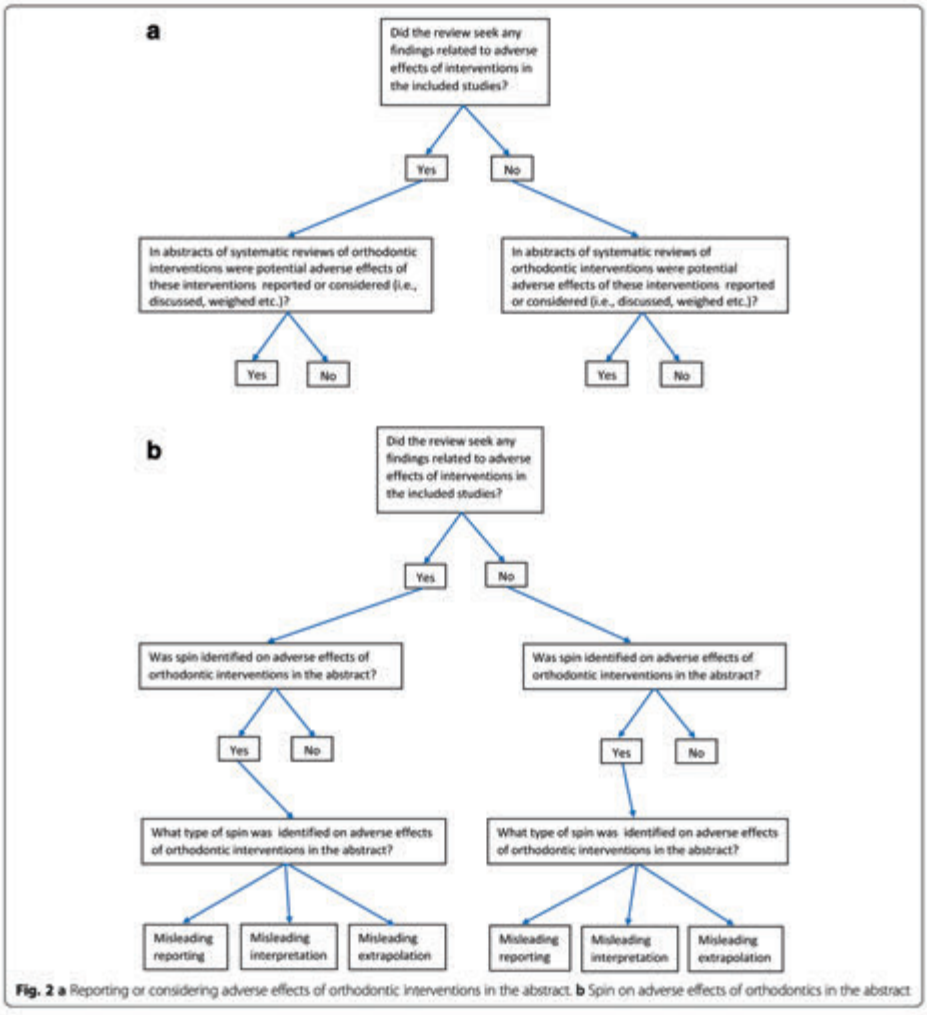


**Fig. 2 a** Reporting or considering adverse effects of orthodontic interventions in the abstract. **b** Spin on adverse effects of orthodontics in the abstract

**Table 5** Summary of findings

| Description of outcomes from the main text | Statistic |
|---|---|
| The number of retrieved systematic reviews | Number |
| The number of eligible systematic reviews | Number |
| The prevalence of eligible systematic reviews | Prevalence |
| The prevalence of eligible systematic reviews that did seek any findings related to adverse effects of interventions in the included studies | Prevalence |
| The prevalence of eligible systematic reviews in which potential adverse effects of these interventions were reported or considered (i.e., discussed, weighed, etc.) in the abstract* | Prevalence |
| The prevalence of eligible systematic reviews in which spin was identified on adverse effects of orthodontic interventions in the abstract* | Prevalence |
| The prevalence of misleading reporting-related spin in the abstract* | Prevalence |
| The prevalence of misleading interpretation-related spin in the abstract* | Prevalence |
| The prevalence of misleading extrapolation-related spin in the abstract* | Prevalence |

**All prevalence data will be presented with their 95% confidence intervals**
***This statistic will be reported for reviews that sought and did not seek any findings related to adverse effects of interventions in the included studies**

## Discussion

### Strengths

Key strengths of this research study include the following: (1) we conducted extensive scoping searches and pilot studies to fine-tune our research questions and methods. These activities confirmed the importance of our questions. (2) Our research team consists of two topic experts (PS and RMR) and two methodologists (RMR and NDG). (3) All study selection and data collection procedures will be undertaken independently by two authors (PS and RMR). Calibration of these operators was done during the pilot studies. (4) To guarantee reproducibility and full access to our data, we will publish our protocol a priori and will include all raw data of the completed research study in additional files or will deposit them in an open-access repository [43–45, 47].

### Limitations

Including only orthodontic intervention reviews published in the five leading orthodontic journals and in the Cochrane Database of Systematic Reviews could be a limitation, but we expect that the findings in this subgroup of journals will underestimate the true severity of spin on adverse effects of interventions in the abstracts of these reviews. Including only reviews published in the last 10 years could also be a limitation. However, we chose this period because it brings the current knowledge status on our research questions to the foreground and these 10 years coincide with the launch in 2009 of the checklist of Preferred Reporting Items for Systematic Reviews and Meta- Analyses (PRISMA) [32, 33].

### Importance and beneficiaries

In this research study, we will address three key questions in abstracts of systematic reviews of orthodontic interventions: whether potential adverse effects of these interventions were reported or considered, whether spin was identified regarding information on these adverse effects, and the type of spin. These issues are important, because (1) the assessment and

reporting of adverse effects of interventions is often suboptimal [7–11], (2) titles and abstracts are the most read sections of papers in the biomedical literature [1], (3) a high prevalence of spin has been identified in abstracts of both randomized and non-randomized studies [4, 21], and (4) incomplete or inadequate reporting, interpretation, or extrapolation of findings on adverse effects in the abstract can mislead readers and could lead to inadequate practice [4]. Our results will raise the awareness of considering adverse effects and the phenomenon of spin regarding these effects in abstracts of systematic reviews of orthodontic interventions. Patients, clinicians, researchers, editors, peer-reviewers, guideline developers, policy makers, and research funders will all be beneficiaries of the findings of this research study.



## Supplementary information

Supplementary information accompanies this paper at https://doi.org/10. 1186/s41073-019-0084-4.

**Additional file 1.** Checklist for the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) 2015 statement.
**Additional file 2.** Pilot tests.
**Additional file 3.** Search terms and their derivatives.
**Additional file 4.** Data collection forms.

**Abbreviations**
MECIR: Methodological Expectations of Cochrane Intervention Reviews;
PRISMA: Preferred reporting items for systematic reviews and meta-analyses;
PRISMA-P: Preferred Reporting Items for Systematic review and Meta- Analysis-Protocols

**Acknowledgements**
Not applicable

**Authors' contributions**
PS and RMR conceived and designed the study protocol for this cross-sectional study. RMR is the guarantor. PS and RMR conducted the pilot testing of the study selection procedures and data extraction forms and fine-tuned the research protocol after the pilot testing. NDG provided support on methodological and statistical issues and assisted in the overall fine-tuning of this protocol. All three authors read and approved the final protocol.

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All expenses for preparing this protocol and for conducting the subsequent research study will be paid evenly by each author.

**Availability of data and materials**
Not applicable

**Ethics approval and consent to participate**
Not applicable

**Consent for publication**
Not applicable

**Competing interests**
The authors declare that they have no competing interests.

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**Publisher's Note**

# CHAPTER 5

## Spin on adverse effects in abstracts of systematic reviews of orthodontic interventions: a cross-sectional study (part 2)

This is a non-edited version of the manuscript:

Steegmans PAJ, Di Girolamo N, Meursinge Reynders RA. Spin on adverse effects in abstracts of systematic reviews of orthodontic interventions: a cross-sectional study (part 2). Syst Rev. 2023 Jun 20;12(1):99.

## Abstract

**Background** It is critical that abstracts of systematic reviews transparently report both the beneficial and adverse effects of interventions without misleading the readers. This cross-sectional study assessed whether adverse effects of interventions were reported or considered in abstracts of systematic reviews of orthodontic interventions and whether spin on adverse effects was identified when comparing the abstracts with what was sought and reported in these reviews.

**Methods** This cross-sectional study (part 2 of 2) used the same sample of 98 systematic reviews orthodontic interventions as used in part 1. Eligible reviews were retrieved from the Cochrane Database of Systematic Reviews and the 5 leading orthodontic journals between August 1 2009 and July 31 2021. Prevalence proportions were sought for 3 outcomes as defined in the published protocol. Univariable logistic regression models were built to explore associations between the presence of spin in the abstract and a series of predictors. Odds ratios (OR) 95% confidence intervals (95% CI) were used to quantify the strength of associations and their precision.

**Results** 76.5% (75/98) of eligible reviews reported or considered (i.e., discussed, weighted etc.) potential adverse effects of orthodontic interventions in the abstract and the proportion of spin on adverse effects was 40.8% (40/98) in the abstract of these reviews. Misleading reporting was the predominant category of spin, i.e., 90% (36/40). Our explorative analyses found that compared to the Cochrane Database of Systematic Reviews all 5 orthodontic journals had similar odds of the presence of spin on adverse effects in abstracts of systematic reviews of orthodontic interventions. The odds of the presence of spin did not change over the sampled years (OR: 1.03, 95% CI: 0.9 to 1.16) and did not depend on the number of authors (OR: 0.93, 95% CI: 0.71 to 1.21), or on the type of orthodontic intervention (OR: 1.1, 95% CI: 0.45 to 2.67), or whether conflicts of interests were reported (OR: 0.74, 95% CI: 0.32 to 1.68).

**Conclusion** End users of systematic reviews of orthodontic interventions have to be careful when interpreting results on adverse effects in the abstracts of these reviews, because they could be jeopardized by uncertainties such as not being reported and misleading reporting as a result of spin.

**Keywords** Orthodontics, Reporting, Systematic review, Intervention, Spin, Misleading reporting, Misleading interpretation, Misleading extrapolation, Adverse effect, Adverse event, Harm, Safety

## Background

Abstracts should provide key information on a research study, which helps readers decide whether or not to access the full report [1]. It is therefore critical that abstracts transparently report the results of both the beneficial and adverse effects of interventions without misleading the readers. Misleading reporting, misleading interpretation, and misleading extrapolation of study results has been called "spin" [2, 3]. In this study, we assessed whether adverse effects of interventions were reported or considered in abstracts of both Cochrane and non-Cochrane reviews of orthodontic interventions and whether spin and what type of spin regarding adverse effects was present when comparing the abstracts with what was sought and reported in these reviews.

Titles and abstracts of publications of healthcare interventions are used for multiple purposes such as (1) an initial screening of the study type; (2) clarifying the included type of patients, interventions, comparators, outcomes, and settings; (3) obtaining a summary of the findings; and (4) an initial assessment of the validity of the study [1, 4, 5]. Titles and abstracts are the most and often only read sections of biomedical papers, because of a lack of time of readers, paywalls, or language issues [6]. It is therefore important that abstracts can be used as stand-alone documents that clearly and truthfully reflect what was reported in the full text [7]. The standard for Methodological Expectations of Cochrane Intervention Reviews (MECIR) [8] states under Item R13 that "The abstract of the review should aim to reflect a balanced summary of the benefits and harms of the intervention" and this is a "mandatory" Cochrane review standard. The inclusion of 'adverse effects' in this standard is crucial, because these effects are often poorly assessed and reported in clinical trials and systematic reviews of healthcare interventions [9–16].

In this context, it is important that findings on adverse effects are presented accurately in the abstract without misleading the reader. "A distorted presentation of study results" has been called "spin" [2, 3]. This definition and other commonly used definitions of spin and key terminology used in this article are listed in Table 1 [2, 3, 17–25].

Spin has been subdivided in 3 categories: "misleading reporting," "misleading interpretations," and "misleading extrapolations" of study results [2]. We adopted the definitions by Lazarus et al. [23] for these 3 categories of spin (Table 1). Controlling spin is important, because of its high prevalence and its consequences. For example, a randomized controlled trial (RCT) showed that spin in abstracts can influence the clinician's interpretation of the results of a study [26]. Further, Yavchitz et al. [27] showed that the presence of spin in press releases and the mass media was related with spin in the conclusions of the pertinent abstracts of peer-reviewed RCTs. Our scoping searches showed that a high prevalence of spin has been recorded in abstracts of numerous research studies and for a wide variety of disciplines. For example, spin was present in 84% (107/128) of abstracts of reports of non-randomized studies assessing an intervention [23], 23% (24/105) of abstracts of RCTs in rheumatology [28], 57% (53/93) of abstracts of cardiovascular RCT reports [29], 34.2% (25/73) of abstracts of systematic reviews and meta-analyses related to treatment of proximal humerus fractures [30], 37.6% (27/72) of results, and 58.3% (42/72) of conclusions of abstracts of parallel-group RCTs with statistically non-significant results ($P \geq 0.05$) [25]. Spin in abstracts of orthodontic studies was assessed in 2 recent publications

[31, 32]. Guo et al. [31] found spin in 62.2% (69/111) of abstracts of parallel-group RCTs with clearly stated statistically non-significant primary outcomes and Makou et al. [32] identified spin in 48.6% (53/109) of abstracts of orthodontic meta-analyses.

This is part 2 of 2 cross-sectional studies on assessing and reporting of adverse effects in systematic reviews of orthodontic interventions published in 5 leading orthodontic journals and in the Cochrane Database of Systematic Reviews. Part 1 focused predominantly on seeking and reporting of adverse effects in the main text and supplementary files of these reviews [18, 33]. In part 2, we assessed whether adverse effects of orthodontic interventions were reported or considered (i.e., discussed, weighed etc.) in abstracts of these reviews. We further measured whether spin was introduced in the abstract regarding information on adverse effects as found and reported in these reviews. We also assessed the different categories of spin. The findings of this research study are important not only for patients and clinicians but also for researchers, peer reviewers, and editors because they have a crucial role in reducing the prevalence of spin [34].

**Table 1** Glossary of terms

| Term | Definition |
|---|---|
| Systematic review | Cochrane [17] defines a systematic review as follows: "A systematic review attempts to identify, appraise and synthesize all the empirical evidence that meets pre-specified eligibility criteria to answer a specific research question. Researchers conducting systematic reviews use explicit, systematic methods that are selected with a view aimed at minimizing bias, to produce more reliable findings to inform decision making." |
| Intervention review | Cochrane [17] defines an intervention review as follows: "Intervention reviews assess the effectiveness/safety of a treatment, vaccine, device, preventative measure, procedure or policy." |
| Orthodontic interventions | Steegmans et al. [18] define orthodontic interventions as follows: "Orthodontic interventions refer to the use of *any* type of orthodontic appliance to move teeth or change the jaw size or position for orthodontic purposes. These interventions also include appliances to maintain or stabilize the results of orthodontic treatment, for example retainers." |
| Adverse effect | Cochrane [19, 20] defines an adverse effect as "an adverse event for which the causal relation between the intervention and the event is at least a reasonable possibility." |
| Spin [3] | "Distorted presentation of study results." |
| Spin [3] | "A misrepresentation of study results, regardless of motive (intentionally or unintentionally) that overemphasizes the beneficial effects of the intervention and overstates safety compared with that shown by the results." |
| Spin [21] | "A specific intentional or unintentional reporting that fails to faithfully reflect the nature and range of findings and that could affect the impression the results produce in readers" |
| Spin [22] | "A specific reporting that fails to faithfully reflect the nature and range of findings and that could affect the impression that the results produce in readers, a way to distort science reporting without actually lying" |
| Misleading reporting related spin [23] | "Incomplete reporting of the study results that could be misleading for the reader." |
| Misleading interpretation related spin [23] | Inadequate interpretation of the study results overestimating the beneficial effect of the intervention. |
| Misleading (inappropriate) extrapolation related spin [23] | Inappropriate generalization of the study results by inadequate (1) extrapolation from the population, interventions, or outcome actually assessed in the study to a larger population, different interventions, or outcomes or (2) inadequate implications for clinical practice. |
| Spin (in the abstract) on adverse effects of interventions [24] | Incomplete or inadequate reporting, interpretation, or extrapolation (or a combination of these variables) of findings on adverse effects of interventions in the abstract that could be misleading for the reader. |

## Objectives

Our objectives were presented in the following 3 research questions [24]. Recent (up to October 31, 2021) scoping searches showed that these questions were not assessed previously.

• Question 1. In abstracts of systematic reviews of orthodontic interventions, were potential adverse effects of these interventions reported or considered (i.e., discussed, weighed etc.)?

• Question 2. Was spin identified on adverse effects of orthodontic interventions in the abstract?

• Question 3. What type of spin was identified on adverse effects of orthodontic interventions in the abstract?



## Methods

This manuscript reports the methods and results of part 2 of a cross-sectional study using the same 98 eligible reviews as in part 1 [33]. Additional information on the research methods and the characteristics of the included reviews can be found in part 1 [33] and in the published protocols of parts 1 and 2 [18, 24]. The protocol for this second cross-sectional study was published in "Research Integrity and Peer Review" [24] and can be consulted via the following link: https://researchintegrityjournal.biomedcentral.com/articles/10.1186/s41073-019-0084-4.

The checklist of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cross-sectional studies [35] was included as Additional file 1. The differences between the methods planned in our protocol and those implemented in the final study were reported in Additional file 2. The rationales for these differences were also given. All raw data were reported in the Open Science framework Open Science Framework (https://osf.io/ka7mp/). There was no patient or public involvement during the development of the protocol or in the conduct of this study. The eligibility criteria, information sources, search strategy, and selection process used in part 1 of this cross-sectional study [33] were also used for part 2 of this study. To reduce the need of cross-checking between manuscripts, we reported these sections again.

### Eligibility criteria

The eligibility criteria were published previously in our protocol [24] and in part 1 of this study [33] and were developed by two researchers (PS and RMR). These criteria are presented in Table 2 [36] and are further explained under here.

***Study designs***

• We included systematic reviews of orthodontic interventions. The definitions of the terms "systematic review," "intervention review," and "orthodontic interventions" listed in the Glossary of terms (Table 1) were used to assess eligibility.

• The following reviews were excluded: (1) noninterventional reviews such as "Methodology," "Diagnostic," "Qualitative," and "Prognostic"; (2) rapid and scoping reviews; (3) systematic reviews with Bayesian network meta-analysis; and (4) systematic reviews of interventions that did not find any eligible studies (empty reviews).

***Participants***

- Systematic reviews of interventions on any type of patients undergoing orthodontic interventions, i.e., patients of any health status, sex, age, and demo graphics, and socio-economic status were eligible.
- Intervention reviews that focused exclusively on patients with congenital anomalies, for example, with cleft lip and palate and systematic reviews of animal or laboratory studies were excluded.

***Interventions***

- Systematic reviews on the following interventions were eligible: (1) systematic reviews that assessed the effects of clinical orthodontic interventions. Clinical orthodontic interventions refer to any type of orthodontic appliance that are used to move teeth or change the jaw size or position for orthodontic purposes; (2) systematic reviews of interventions with appliances to maintain or stabilize the outcomes of orthodontic treatment, for example, retainers; (3) systematic reviews of orthodontic interventions that compared the effects of orthodontic treatment with or without additional interventions such as pharmacological or small surgical interventions, e.g., periodontal or implant surgery; and (4) no exclusion criteria were applied to the characteristics of the operator who conducted the interventions.
- Systematic reviews on the following interventions were excluded: (1) systematic reviews in which patients receive orthodontic treatment, but in which the effects of other interventions, e.g., periodontal surgery, were compared and not the effects of orthodontic interventions; (2) systematic reviews of interventions in which orthodontic appliances were specifically used for other purposes, e.g., changing jaw positions to treat respiration or temporomandibular disorders; (3) systematic review of orthodontic interventions that included orthognathic surgery; (4) systematic reviews that focused exclusively on adverse effects of interventions; and (5) systematic reviews that did not assess a specific orthodontic intervention but referred to orthodontic treatment as a whole.

***Outcomes***

- Systematic reviews of orthodontic interventions that assessed any adverse effect of orthodontic interventions scored at any endpoint or timing were eligible. The effects

of orthodontic interventions did not refer just to outcomes related to tooth and jaw size and positions but also to broader outcomes such as periodontal health, esthetic changes, the health of the temporomandibular joint, patient health experiences, and economic issues associated with the interventions. The reporting of outcomes on adverse effects did not determine eligibility of reviews for this cross-sectional study, i.e., reviews were not excluded because they did not report measured outcome data in a "usable" way [36].

- No exclusion criteria regarding the outcomes of systematic reviews of orthodontic interventions were applied.

***Setting***

• Systematic reviews of orthodontic interventions that reported on interventions conducted in any type of setting, i.e., university or private practice, were eligible.



**Table 2** Eligibility criteria

| Item | Included | Excluded |
|---|---|---|
| **Study designs** | Systematic reviews of orthodontic interventions. The definition of systematic review, intervention review, and orthodontic interventions listed in the Glossary of terms will be used to assess whether a review is eligible (Table 1). | 1) Noninterventional reviews such as "Methodology," "Diagnostic," "Qualitative," and "Prognostic"<br>2) Rapid and scoping reviews<br>3) Systematic reviews with Bayesian network meta-analysis<br>4) Systematic reviews of interventions that did not find any eligible studies (empty reviews) |
| **Participants** | Systematic reviews on any type of patients undergoing orthodontic interventions, i.e., patients of any health status, sex, age, and demographics, and socio-economic status. | 1) Intervention reviews that focus exclusively on patients with congenital anomalies, for example with cleft lip and palate<br>2) Systematic reviews of animal or laboratory studies |
| **Interventions** | 1) Systematic reviews that assessed the effects of clinical orthodontic interventions. Clinical orthodontic interventions refer to any type of orthodontic appliance that are used to move teeth or change the jaw size or position for orthodontic purposes<br>2) Systematic reviews of interventions with appliances to maintain or stabilize the outcomes of orthodontic treatment, for example retainers<br>3) Systematic reviews of orthodontic interventions that compared the effects of orthodontic treatment with or without additional interventions such as pharmacological or small surgical interventions, e.g., periodontal or implant surgery<br>4) No exclusion criteria were applied to the characteristics of the operator who conducted the interventions | 1) Systematic reviews in which patients receive orthodontic treatment, but in which the effects of other interventions, e.g., periodontal surgery, were compared and not the effects of orthodontic interventions<br>2) Systematic reviews of interventions in which orthodontic appliances were specifically used for other purposes, e.g., changing jaw positions to treat respiration or temporomandibular disorders<br>3) Systematic review of orthodontic interventions that included orthognathic surgery<br>4) Systematic reviews that focused exclusively on adverse effects of interventions<br>5) Systematic reviews that did not assess a specific orthodontic intervention but referred to orthodontic treatment as a whole |
| **Outcomes** | 1) Any adverse effect of orthodontic interventions scored at any endpoint or timing<br>2) The effects of orthodontic interventions did not refer just to outcomes related to tooth and jaw size and positions but also to broader outcomes such as periodontal health, esthetic changes, the health of the temporomandibular joint, patient health experiences, and economic issues associated with the interventions<br>3) The reporting of outcomes on adverse effects did not determine eligibility of reviews for this cross-sectional study, i.e., reviews were not excluded because they did not report measured outcome data in a "usable" way [36]. | No exclusion criteria |
| **Stetting** | Any type of setting in which the interventions were conducted, i.e., university or private practice etc. | No exclusion criteria |

**Information sources and search strategy**

The Cochrane Database of Systematic reviews [37] and the websites of 5 leading orthodontic journals were the information sources of this study. The journal selection of the latter journals was based on two criteria: (1) the journal has been published for 10 years or more

and (2) the highest impact factor. The following 5 orthodontic journals fulfilled these criteria: European Journal of Orthodontics [EJO], American Journal of Orthodontics and Dentofacial Orthopedics [AJODO], Angle Orthodontist (AO), The Korean Journal of Orthodontics (KJO), and Orthodontics and Craniofacial Research (OCR). These journals were manually searched from August 1, 2009, until July 31, 2021, for systematic reviews that fulfilled the eligibility criteria. August 1, 2019, was chosen as the starting date, because it coincides with the launch of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement on 21 July 2009 [38, 39].

**Study records**

***Selection process***

Two reviewers (PS and RMR) manually searched systematic reviews that fulfilled the eligible criteria. Pilot tests were conducted a priori to train both reviewers and to calibrate them. All titles and abstracts in the websites of the 5 orthodontic journals were hand-searched for eligible reviews. Eligible Cochrane reviews were searched in the section "Dentistry and Oral health" in the Cochrane library. Only the latest version of a review was eligible when review updates had been published. In the case of disagreement on the selection procedures, the following strategies were implemented and in this sequence: (1) discussions between these operators, (2) rereading the paper, (3) contacting of authors by email to clarify issues regarding a specific manuscript. Persistent disagreements were resolved through consultation with a methodologist. A total of 98 eligible systematic reviews of orthodontic interventions was identified in part 1 of this study [33]. This same sample of 98 studies was also used in this study.

***Data collection procedures***

All 98 eligible reviews together with their supplemental files were merged into binder PDFs, and according to protocol [24], pertinent search terms were linked to these documents to facilitate data extraction (Additional file 2). Our pilot-tested data collection forms were used to extract data and are given in Additional file 2. Data items were collected from the entire eligible review, i.e., the entire manuscript including the abstract, tables, figures, and additional files. We implemented this procedure for all eligible reviews but did not extract data from the plain language summary of eligible Cochrane reviews. Two calibrated authors (PS and RMR) independently collected data from the 98 eligible reviews to address the research questions. In the case of disagreement, we applied the same strategies as reported in the section "Selection process" and the third author (NDG) was consulted in the case of persistent disagreements.

***Assessing adverse effects of orthodontic interventions***

Pain and the various categories of adverse effects hypothetically linked to orthodontic interventions as defined by Preoteasa et al. [40] and modified by Steegmans et al. [33] were reported in a table in Additional file 2. This table was consulted as our reference to assess the reporting on adverse effects in the abstract. When additional adverse effects were identified that were not given in this table, we included them with rationale. Effects that

could be labeled either as “beneficial” or “adverse” were not included unless the review authors labeled these ambiguous effects as “adverse.” Explanations for such decisions were given. Orthodontic interventions were classified in three types, i.e., type 1: orthodontic interventions to move teeth or change the jaw size or position for orthodontic purposes, type 2: orthodontic interventions with additional surgical, pharmacological, or vibratory interventions, and type 3: orthodontic interventions to maintain or stabilize orthodontic results.

### *Assigning spin of adverse effects of orthodontic interventions in abstracts of systematic reviews*

Spin was assigned by comparing whether what was reported in the abstract on adverse effects of orthodontic interventions was congruent with the findings on these effects in the review. Three types of spin were assigned i.e., misleading reporting, misleading interpretation, and misleading (inappropriate) extrapolation on adverse effects of orthodontic interventions in abstracts of systematic reviews [27]. To facilitate this assignment and to reduce the risk of misinterpretation, each type of spin was subdivided in categories. The presence of spin was assigned when it was identified in one or more of these categories. Spin was assessed in all eligible reviews irrespective of whether these reviews sought adverse effects of interventions or not. Because the pilot tests for our protocol identified only 2 reviews with spin [24] and because assessing spin is not easy [22], we conducted additional pilot tests on 10 RCTs to further calibrate the operators (PS and RMR) that assigned spin and to fine-tune the descriptions of spin and the checklists for assigning spin. These fine-tuned descriptions of the different types of spin and the pertinent data collection forms to identify spin are reported respectively in Table 3 and Additional file 2. Definitions of spin were given for reviews that sought and those that did not seek adverse effects of orthodontic interventions (Table 3).

**Table 3** Types of spin in reviews that did or did not seek adverse effects of interventions

| Definitions of the 3 types of spin | Reviews that sought adverse effects of interventions | Reviews that did not seek adverse effects of interventions |
|---|---|---|
| **Misleading reporting (in the abstract) on adverse effects of interventions:**<br>“Incomplete or inadequate reporting in the abstract on the results of adverse effects that were not supported by the findings of the review” | **Categories:**<br>1) Not reporting in the abstract on the results of adverse effects found in the review.<br>2) Selective reporting in the abstract on the results of adverse effects found in the review. | **Categories:**<br>1) Reporting on results of adverse effects in the abstract when adverse effects were not sought.<br>2) Reporting in the abstract that adverse effects were sought when they were not sought. |
| **Misleading interpretation (in the abstract) on adverse effects of interventions:**<br>“Interpretation in the abstract on the results of adverse effects that was not supported by the findings of the review.” This could for example underestimated the adverse effects of the intervention. | **Categories:**<br>1) Claiming in the abstract that the intervention is safe (has no or minimal adverse effects), despite concerning results on adverse effects found in the review, e.g., based on non-statistically significant results on adverse effects with wide confidence intervals [27].<br>2) Downgrading in the abstract the importance of the adverse effects, despite concerning results on adverse effects found in the review.<br>3) Recommendations are made in the abstract for clinical practice that are not supported by the findings in the review on adverse effects [27]. | **Categories:**<br>1) Claiming in the abstract that the intervention is safe (has no or minimal adverse effects) despite not having sought adverse effects.<br>2) Downgrading in the abstract the importance of the adverse effects, despite not having sought adverse effects.<br>3) Recommendations are made in the abstract for clinical practice despite not having sought adverse effects. |
| **Misleading (inappropriate) extrapolation (in the abstract) on adverse effects of interventions:**<br>“Overgeneralisation in the abstract of the study results to different populations, interventions, outcomes or settings than were assessed in the review despite evidence on adverse effects on a different population, intervention, outcome or setting.” | **Categories:**<br>1) Results are extrapolated in the abstract to another population, intervention, outcome, or setting than were assessed in the review despite evidence on adverse effects on a different population, intervention, outcome, or setting. | **Categories:**<br>1) Results are extrapolated in the abstract to another population, intervention, outcome, or setting than were assessed in the review despite not having sought adverse effects. |

***Power calculation***

In our pilot sample, we identified an overall proportion of 14.3% (2/14) of spin of the adverse effects in the abstracts of 14 systematic reviews of orthodontic interventions. For this proportion, the Epitools software [41] calculated a required sample size of 48 studies (precision 0.1 and confidence level 0.95), which was fulfilled by our 98 eligible reviews.

**Outcomes and statistical analyses**

***Outcomes***

Prevalence proportions were calculated to quantify the answers to our 3 research questions in the 98 selected reviews. According to our published protocol, these proportions were also calculated separately for reviews that either did (*n* = 84) or did not (*n* = 14) seek any findings related to adverse effects of interventions in the included studies [33]. These statistics were calculated for (1) all journals as a one group, (2) the five leading orthodontic journals together and the Cochrane Database of Systematic Reviews separately, and (3) each eligible journal separately.

***Explorative analyses***

Univariable logistic regression models were built to determine the association between the presence of spin in the abstract and characteristics of the systematic review, i.e., journal, year of publication, number of authors, conflict of interest reported, conflict of interest present, funding reported, and type of orthodontic intervention. These analyses were not registered in the protocol and should therefore be interpreted as exploratory. The strengths of associations were quantified using odds ratios (OR) and 95% confidence intervals (95% CI). Multivariable models were built if multiple significant predictors were found in the univariable analysis. Analyses were performed with the use of commercial software (IBM SPSS 22.0, SPSS Inc, Chicago, IL). A two-sided *P* value of 0.05 was considered to be statistically significant.

## Results

The results of the search for eligible reviews were reported previously in part 1 of this cross-sectional study [33] and identified 98 eligible reviews. The PRISMA flow diagram and all included reviews and all excluded studies with rationale were given again in Additional file 3. Figures 1 and 2 present the flow diagrams of the answers to the research questions, and Tables 4 and 5 report the pertinent proportion statistics. The number of identified systematic reviews and the number of eligible systematic reviews of orthodontic interventions given in these tables were published previously [33] and were reported again to give context to the outcomes to our research questions. In these tables, outcomes are further subdivided for eligible reviews that did (*n* = 84) or did not (*n* = 14) seek any findings related to adverse effects of interventions in the included studies. The initial inter-operator agreement between both operators for assigning spin was high (Cohen's $\kappa$ = 0.94), and complete agreement between operators was reached after discussion.

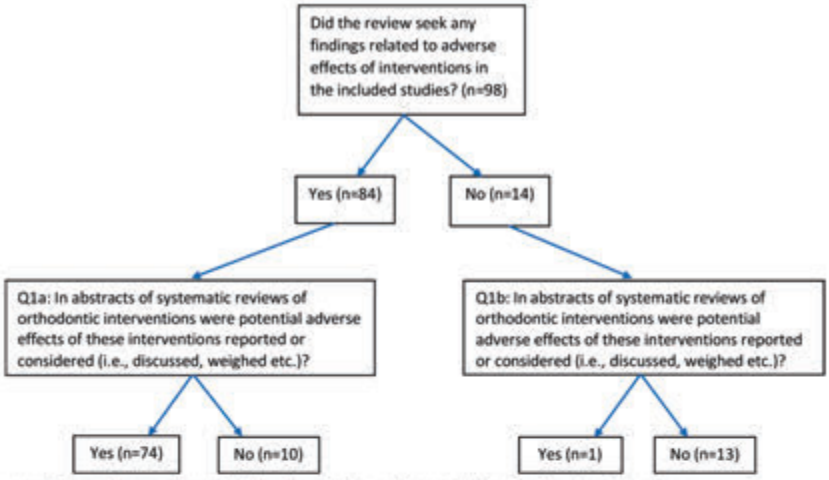


**Fig. 1** Reporting or considering adverse effects of orthodontic interventions in abstracts of systematic reviews



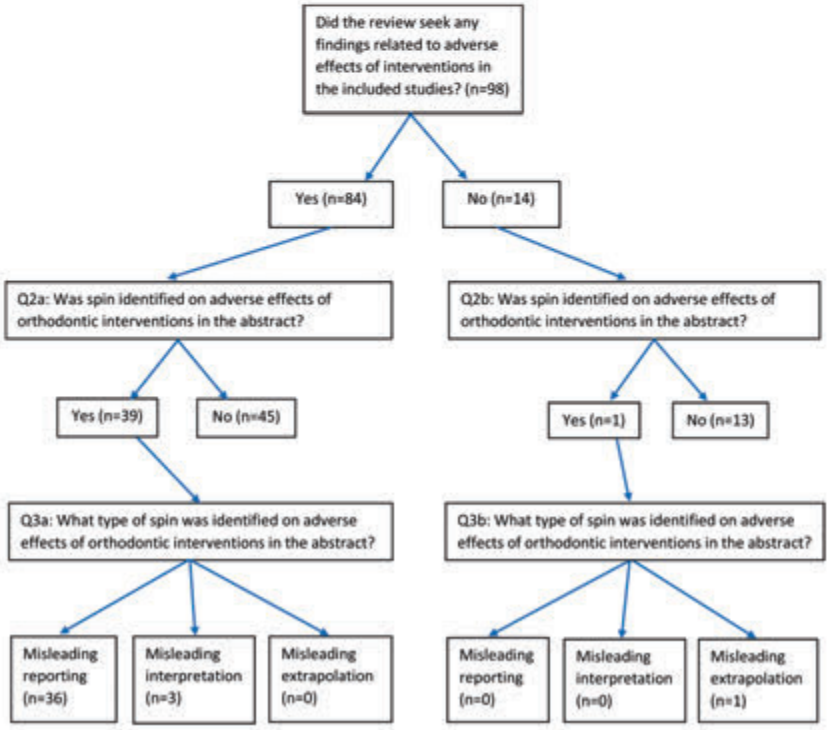


**Fig. 2** Spin on adverse effects of orthodontic interventions in abstracts of systematic reviews

**Results for questions 1a and 1b**

The results for questions 1a and 1b combined showed that the majority 76.5% (75/98) of eligible reviews reported or considered (i.e., discussed, weighted etc.) potential adverse effects of orthodontic interventions in the abstract (Fig. 1). This prevalence was much higher in the reviews that sought any findings related to adverse effects of interventions in the included studies (88.1% (74/84) than those reviews that did not seek these findings (7.1% (1/14) (Fig. 1).

**Results for questions 2a and 2b**

The results for questions 2a and 2b combined showed that the total proportion of the presence of spin on adverse effects in the abstract was 40.8% (40/98) in the eligible reviews (Table 4). This prevalence was considerable higher in the reviews that sought any findings related to adverse effects of interventions in the included studies (Question 2a), i.e., 46.4% (39/84) than those reviews that did not seek such findings 7.1% (1/14) (Fig.2).

**Results for questions 3a and 3b**

For questions 3a and 3b combined, misleading reporting was the predominant type of spin i.e., 90% (36/40), which was subdivided in the categories of not reporting, 32.5% (13/40), and selective reporting 57.5% (23/40) (Table 5). Misleading interpretation and misleading (inappropriate) extrapolation types of spin were respectively 7.5% (3/40) and 2.5% (1/40).

**Table 4** Outcomes on reporting or considering adverse effects and spin in abstracts of systematic reviews of orthodontic interventions

| Description of outcomes | Cochrane | EJO | AJODO | AO | KJO | O&CR | All orthodontic journals | All journals |
|---|---|---|---|---|---|---|---|---|
| The number of identified systematic reviews | *n* = 29 | *n* = 100 | *n* = 68 | *n* = 61 | *n* = 11 | *n* = 53 | *n* = 293 | *n* = 322 |
| The number of eligible systematic reviews of orthodontic interventions | *n* = 10 | *n* = 28 | *n* = 20 | *n* = 23 | *n* = 3 | *n* = 14 | *n* = 88 | *n* = 98 |
| The prevalence of eligible systematic reviews of orthodontic interventions that sought any findings related to adverse effects of interventions in the included studies[a] | 100.0% (10/10) | 92.9% (26/28) | 75.0% (15/20) | 78.3% (18/23) | 100.0% (3/3) | 85.7% (12/14) | 84.1% (74/88) | 85.7% (84/98) |
| Outcome 1: The prevalence of eligible systematic reviews in which potential adverse effects of interventions were reported or considered (i.e., discussed, weighted etc.) in the abstract[a] | 100.0% (10/10) | 82.1% (23/28) | 65.0% (13/20) | 65.2% (15/23) | 100.0% (3/3) | 78.6% (11/14) | 73.9% (65/88) | 76.5% (75/98) |
| Outcome 1a: The prevalence of eligible systematic reviews in which potential adverse effects of interventions were reported or considered (i.e., discussed, weighted etc.) in the abstract[a] | 100% (10/10) | 88.5% (23/26) | 86.7% (13/15) | 77.8% (14/18) | 100% (3/3) | 91.7% (11/12) | 86.5% (64/74) | 88.1% (74/84) |
| Outcome 1b: The prevalence of eligible systematic reviews in which potential adverse effects of interventions were reported or considered (i.e., discussed, weighted etc.) in the abstract[a] | 00.0% (0/0) | 0.0% (0/2) | 0.0% (0/5) | 20.0% (1/5) | 0.0% (0/0) | 0.0% (0/2) | 7.1% (1/14) | 7.1% (1/14) |
| Outcome 2: The prevalence of eligible systematic reviews in which spin was identified on adverse effects of orthodontic interventions in the abstract[a] | 60.0% (6/10) | 35.7% (10/28) | 30.0% (6/20) | 39.1% (9/23) | 66.7% (2/3) | 50.0% (7/14) | 38.6% (34/88) | 40.8% 40/98 |

**Table 4** (continued)

| Description of outcomes | Cochrane | EJO | AJODO | AO | KJO | O&CR | All orthodontic journals | All journals |
|---|---|---|---|---|---|---|---|---|
| Outcome 2a: The prevalence of eligible systematic reviews in which spin was identified on adverse effects of orthodontic interventions in the abstract[a] | 60.0% (6/10) | 38.5% (10/26) | 40.0% (6/15) | 44.4% (8/18) | 66.7% (2/3) | 58.3% (7/12) | 44.6% (33/74) | 46.4% (39/84) |
| Outcome 2b: The prevalence of eligible systematic reviews in which spin was identified on adverse effects of orthodontic interventions in the abstract[a] | 0.0% (0/0) | 0.0% (0/2) | 0.0% (0/5) | 20.0% (1/5) | 0.0% (0/0) | 0.0% (0/2) | 7.1% (1/14) | 7.1% (1/14) |

[a] Outcome 1a addresses research question 1a, outcome 1b addresses research question 1b, and outcome 1 addresses the answers to questions 1a and 2b combined, outcome 2a addresses research question 2a, outcome 2b addresses research question 2b, and outcome 2 addresses the answers to questions 2a and 2b combined (see Figs. 1 and 2)

**Table 5** Outcome 3: types and categories of spin in abstracts of systematic reviews of orthodontic interventions

| Type of spin and category | Cochrane | EJO | AJODO | AO | KJO | O&CR | All orthodontic journals | All journals |
|---|---|---|---|---|---|---|---|---|
| **Misleading reporting**<br>**Category:** Not reporting in the abstract on the results of adverse effects found in the review. | *n*=2 | *n*=3 | *n*=2 | *n*=5 | *n*=0 | *n*=1 | *n*=11<br>Prevalence: 32.4% (11/34) | *n*=13<br>Prevalence: 32.5% (13/40) |
| **Misleading reporting**<br>**Category:** Selective reporting in the abstract on the results of adverse effects found in the review | *n*=4 | *n*=6 | *n*=4 | *n*=2 | *n*=2 | *n*=5 | *n*=19<br>Prevalence: 55.9% (19/34) | *n*=23<br>Prevalence: 57.5% (23/40) |
| **Misleading interpretation**<br>**Category:**<br>Claiming in the abstract that the intervention is safe (has no or minimal adverse effects), despite concerning results on adverse effects found in the review | | *n*=1 | | *n*=1 | | *n*=1 | *n*=3<br>Prevalence: 8.8% (3/34) | *n*=3<br>Prevalence: 7.5% (3/40) |
| **Misleading (inappropriate) extrapolation**<br>**Category:**<br>Results are extrapolated in the abstract to another population, intervention, outcome or setting than were assessed in the review despite evidence on adverse effects on a different population, intervention, outcome or setting. | | | | *n*=1 | | | *n*=1<br>Prevalence: 2.9% (1/34) | *n*=1<br>Prevalence: 2.5% (1/40) |

**Explorative analyses**

The findings of our explorative analysis on the presence of spin on adverse effects in abstracts of systematic reviews of orthodontic interventions were reported in Table 6. Compared to the Cochrane Database of Systematic Reviews, the EJO (OR: 0.37, 95% CI: 0.08 to 1.63), the AJODO (OR: 0.29, 95% CI: 0.06 to 1.39), the AO (OR: 0.43, 95% CI: 0.09 to 1.95), the KJO (OR: 1.33, 95% CI: 0.09 to 20.11), and the O&C (OR: 0.67, 95% CI: 0.13 to 3.45) had similar odds of the presence of spin on adverse effects in abstracts of systematic reviews of orthodontic interventions. The odds of the presence of spin on adverse effects in abstracts of systematic reviews of orthodontic interventions did not change over the sampled years (OR: 1.03, 95% CI: 0.9 to 1.16). The odds of the presence of spin on adverse effects in abstracts of systematic reviews of orthodontic interventions did not change depending on

the number of authors (OR: 0.93, 95% CI: 0.71 to 1.21). Compared to systematic reviews that did not report conflicts of interest, systematic reviews that reported conflicts of interest had similar odds (OR: 0.74, 95% CI: 0.32 to 1.68) of the presence of spin on adverse effects in abstracts of systematic reviews of orthodontic interventions. Systematic reviews on type 1 orthodontic interventions, i.e., orthodontic interventions to move teeth or change the jaw size or position for orthodontic purposes compared with systematic reviews on type 3 orthodontic interventions, i.e., orthodontic interventions to maintain or stabilize orthodontic results had similar odds (OR: 1.1, 95% CI: 0.45 to 2.67) of the presence of spin on adverse effects of orthodontic interventions in abstracts of systematic reviews (Table 6). Intervention type 2, i.e., orthodontic interventions with additional surgical, pharmacological, or vibratory interventions was not included in the analysis since there was only 1 systematic review of this type of intervention.

**Table 6** Associations between presence of spin in the abstract and characteristics of the systematic review

| Item | Variable insertion in the model | Description | Yes (%) | No (%) | OR | Lower 95%CI | Upper 95%CI | *P* value |
|---|---|---|---|---|---|---|---|---|
| **Journal** | **Categorical** | Cochrane | 4 (40.0%) | 6 (60.0%) | 1 | - | - | - |
| | | EJO | 18 (64.3%) | 10 (35.7%) | 0.37 | 0.08 | 1.63 | 0.19 |
| | | AJODO | 14 (70.0%) | 6 (30.0%) | 0.29 | 0.06 | 1.39 | 0.12 |
| | | AO | 14 (60.9%) | 9 (39.1%) | 0.43 | 0.09 | 1.95 | 0.27 |
| | | KJO | 1 (33.3%) | 2 (66.7%) | 1.33 | 0.09 | 20.11 | 0.84 |
| | | O&C | 7 (50.0%) | 7 (50.0%) | 0.67 | 0.13 | 3.45 | 0.63 |
| **Year of publication** | **Continuous** | | | | 1.03 | 0.9 | 1.16 | 0.7 |
| | | 2009 | 1 (100.0%) | 0 (0.0%) | | | | |
| | | 2010 | 1 (33.3%) | 2 (66.7%) | | | | |
| | | 2011 | 5 (71.4%) | 2 (28.6%) | | | | |
| | | 2012 | 2 (100.0%) | 0 (0.0%) | | | | |
| | | 2013 | 6 (66.7%) | 3 (33.3%) | | | | |
| | | 2014 | 3 (33.3%) | 6 (66.7%) | | | | |
| | | 2015 | 9 (75.0%) | 3 (25.0%) | | | | |
| | | 2016 | 5 (55.6%) | 4 (44.4%) | | | | |
| | | 2017 | 5 (55.6%) | 4 (44.4%) | | | | |
| | | 2018 | 6 (46.2%) | 7 (53.8%) | | | | |
| | | 2019 | 3 (75.0%) | 1 (25.0%) | | | | |
| | | 2020 | 7 (58.3%) | 5 (41.7%) | | | | |
| | | 2021 | 5 (62.5%) | 3 (37.5%) | | | | |
| **Number of authors** | **Continuous** | | | | 0.93 | 0.71 | 1.21 | 0.59 |
| | | 2 | 3 (50.0%) | 3 (50.0%) | | | | |
| | | 3 | 7 (50.0%) | 7 (50.0%) | | | | |
| | | 4 | 16 (69.6%) | 7 (30.4%) | | | | |
| | | 5 | 15 (55.6%) | 12 (44.4%) | | | | |
| | | 6 | 8 (53.3%) | 7 (46.7%) | | | | |
| | | 7 | 6 (66.7%) | 3 (33.3%) | | | | |
| | | 8 | 2 (100.0%) | 0 (0.0%) | | | | |
| | | 9 | 1 (50.0%) | 1 (50.0%) | | | | |
| **Conflict of interest reported** | **Categorical** | Yes | 32 (56.1%) | 25 (43.9%) | 0.74 | 0.32 | 1.68 | 0.47 |
| | | No | 26 (63.4%) | 15 (36.6%) | 1 | - | - | - |
| **Conflict of interest present** | | Not reported | 26 (63.4%) | 15 (36.6%) | NA | NA | NA | NA |
| | | No | 32 (56.1%) | 25 (43.9%) | NA | NA | NA | NA |
| **Funding reported** | **Categorical** | Yes | 23 (56.1%) | 18 (43.9%) | 0.8 | 0.35 | 1.81 | 0.6 |
| | | No | 35 (61.4%) | 22 (38.6%) | 1 | - | - | - |
| **Type of orthodontic intervention*** | **Categorical** | 1 | 41 (59.4%) | 28 (40.6%) | 1 | - | - | - |
| | | 2 | 1 (100.0%) | 0 (0.0%) | NA | NA | NA | NA |
| | | 3 | 16 (57.1%) | 12 (42.9%) | 1.1 | 0.45 | 2.67 | 0.84 |

* Type 1 orthodontic interventions: Orthodontic interventions to move teeth or change the jaw size or position for orthodontic purposes. Type 2 orthodontic interventions: Orthodontic interventions with additional surgical, pharmacological, or vibratory interventions. Type 3 orthodontic interventions: Orthodontic interventions to maintain or stabilize orthodontic results

## Discussion

### Principal findings of the study

This cross-sectional study showed that the majority, i.e., 76.5% (75/98), of the eligible systematic reviews reported or considered (i.e., discussed, weighted) potential adverse effects of orthodontic interventions in the abstract (Table 4). In 40.8% (40/98), spin on adverse effects was found in the abstract of these reviews (Table 4). Spin related to misleading reporting was the predominant, i.e., 90.0% (36/40), type of spin (Table 5). No association was found between the presence of spin in the abstract and any of the predictors (Table 6).

### Comparison with other studies

Item 1 of the 2004 CONSORT (Consolidated Standards of Reporting Trials) Harms extension [42] states that "if the study collected data on harms and benefits, the title or abstract should so state". In this second part of our cross-sectional studies, 76.5% (75/98) of systematic reviews reported or considered adverse effects of interventions in the abstracts. This was lower than the 84.7% (83/98) of reviews that sought and reported findings on adverse effects in the main text or supplementary files of these reviews as we reported in part 1 [33]. A recent overview of systematic reviews by Junqueira et al. [43] found that harms were reported in 47% (258/552) of the abstracts of RCTs published prior to the CONSORT harms statement and in 54% (643/1201) of the abstracts of the RCTs published after the publication of this statement, indicating only a limited improvement in recent years. Qureshi et al. [14] found that most systematic reviews 81.4% (57/70) on interventions with gabapentin reported a statement on harms in the abstract. Different results in reporting of adverse effects in abstracts in this cross-sectional study compared with those in other studies could be the result of variables such as differences in (1) research design, i.e., systematic reviews versus RCTs, (2) sample size, (3) what is reported on harms in the abstract, e.g., specific versus more general statements, and (4) the field of research. For example, the relatively high prevalence of reporting of adverse effects in abstracts of systematic reviews in this study could be the result of having included only reviews of orthodontic interventions. Orthodontists might be more attentive in assessing adverse effects, because assessing adverse events such as undesired outcomes of orthodontic treatment and relapse is part of daily clinical practice.

A wide variety of prevalence proportions on spin has been identified in abstracts of systematic reviews of randomized-and non-randomized studies [23, 25, 28–30]. These studies identified proportions of spin that varied between 23% (24/105) of spin in abstracts of RCTs in rheumatology [28] and 84% (107/128) of spin in abstracts of non-randomized studies that assessed interventions [23]. According to our scoping searches, spin in the field of orthodontics has been assessed only in 2 recent studies [31, 32]. Spin was identified in 62.2% (69/111) of abstracts of parallel-group RCTs with clearly stated statistically non-significant primary outcomes [31] and in 48.6% (53/109) of abstracts of orthodontic meta-analyses [32]. In our study, none of the predictors assessed was associated with the presence of spin in this study. Similar findings were identified by Guo et al. [31] on the overlapping predictors with our study, i.e., "the year of publication" and "the number of

authors." Makou et al. [32] also found no association with the presence of spin for the overlapping predictors "journal" and "year of publication" but found a higher risk of spin in studies with a large number of authors (≥ 6). However, direct comparisons of our results on spin and those identified in other studies are often difficult because of differences in variables such as (1) the types and subtypes of spin and definitions of spin, (2) the research design, (3) the locations in the text where spin was assessed, (4) the field of research, (5) the types of interventions, (6) the journals included, and (7) the time point of the publication [42].

**Strengths and limitations**

This study has the following strengths: (1) the research methods were pilot tested on a series of systematic reviews and RCTs to consistently extract data and to calibrate data extractors; (2) the protocol of this study was published a priori; and (3) according to our scoping searches, this is the first study that assessed spin on adverse effects in abstracts of systematic reviews of interventions. These searches also showed that our protocol was the first article [24] that planned to assess spin in the field of orthodontics. Subsequently, 2 additional studies [31, 32] have assessed other types of spin in the orthodontic literature, indicating a growing interest in this topic. (4) All raw data were either included with this manuscript in additional files or registered in Open Science Framework (https://osf.io/ka7mp/).



This study also has limitations such as (1) the risk of inaccurate findings on reporting adverse effects of interventions in abstracts as a result of the inconsistent assessment and reporting of adverse effects in both primary research and in systematic reviews and (2) the assessment of spin is not completely objective [44]. However, our inter-operator agreement was high as indicated by a high Cohen's $\kappa$ (0.94), and disagreements were completely resolved through discussions. (3) The wide variety of different types and definitions of spin and the assessment of spin in different contexts often limits comparing findings on spin between studies [44]. (4) This study assessed a variety of proportions exclusively in Cochrane intervention reviews and in the 5 orthodontic journals with the highest impact factor. Our findings therefore probably underestimate the true magnitude of proportions on poor reporting and spin on adverse effects in the abstracts of the wider body of orthodontic systematic reviews, and (5) the true magnitude of some proportions could also be underestimated, because we assessed a recent sample (August 1, 2009, until July 31, 2021) of reviews. In this context, one should consider that poor reporting has decreased over time as was shown in a study that assessed the evolution of poor reporting in 20,920 RCTs included in a sample of Cochrane reviews [45].

**Implications and future research**

Our results imply that end-users of systematic reviews of orthodontic interventions have to be careful when interpreting the findings on adverse effects in abstracts of both Cochrane reviews and those published in the 5 leading orthodontic journals. This is particularly important, because the title and abstracts are often the only read sections of biomedical papers [6] and spin in abstracts can bias the clinician's interpretations of the results [26]. Reading the full text of research studies is not a solution, because recent studies showed

that the proportions of spin in abstracts are similar to those in the full text of the pertinent RCTs [29] and systematic reviews [46]. Guideline developers, researchers, peer reviewers, and editors have an important role in tackling poor reporting and spin regarding adverse effects in abstracts of systematic reviews of orthodontic interventions. Standards for reporting adverse effects in abstracts of systematic reviews of interventions have to be developed. Much research is ahead.

**Abbreviations**

AJODO American Journal of Orthodontics and Dentofacial Orthopedics
AO Angle Orthodontist
EJO European Journal of Orthodontics
KJO Korean Journal of Orthodontics
O&CR Orthodontics and Craniofacial Research
MECIR Methodological Expectations of Cochrane Intervention Reviews
PRISMA Preferred reporting items for systematic reviews and meta-analyses
RCT Randomized controlled trial
STROBE Strengthening the Reporting of Observational Studies in Epidemiology

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13643-023-02269-3.

**Additional file 1.** STROBE Checklist: Checklist of items that should be included in reports of cross-sectional studies [35].

**Additional file 2.** 2A. Differences between the protocol and the completed cross-sectional study. 2B. Search terms and their derivatives. 2C. Data collection forms. 2D. Adverse effects hypothetically linked to orthodontic interventions.

**Additional file 3.** 3A. PRISMA flow diagram. 3B. Included reviews. 3C. Excluded studies with rationale

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**Authors' contributions**
This cross-sectional study was conceived and designed by PS and RMR. These 2 researchers also conducted all data extraction procedures. PS, RMR, and NDG conducted the data analyses and statistical analyses. NDG provided sup- port on methodological issues. All 3 authors revised the various draft versions of this paper and read and approved the final submitted manuscript. RMR is the guarantor.

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**Availability of data and materials**
Not applicable.

## Declarations

**Ethics approval and consent to participate**
Not applicable.

**Consent for publication**
Not applicable.

**Competing interests**
Reint Meursinge Reynders is an associate editor for *Systematic Reviews*. All three authors declare that they have no further competing interests.

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**Publisher's Note**

# CHAPTER 6

## Fixed orthodontic retainers and periodontal health: a critical appraisal of a systematic review

This is a non-edited version of the manuscript:

Steegmans PAJ, Meursinge Reynders RA. Fixed orthodontic retainers and periodontal health. Evid Based Dent. 2020 Dec;21(4):146-149.

## A commentary on

**Arn M L, Dritsas K, Pandis N, Kloukos D.** The effects of fixed orthodontic retainers on periodontal health: A systematic review. Am J Orthod Dentofacial Orthop 2020; DOI: 10.1016/j.ajodo.2019.10.010.

## Abstract

**Data sources:** The following electronic databases were searched from 1946 to 31 August 2019: Medline, Embase, the Cochrane Oral Health Group's Trials Register, CENTRAL, ClinicalTrials.gov, the National Research Register and Pro-Quest Dissertation Abstracts and Thesis database. **Study selection** The following study designs were eligible: randomised controlled trials (RCTs), controlled clinical trials, cohort studies of prospective and retrospective design, and cross-sectional studies that reported periodontal measurements on patients who received fixed retention after orthodontic therapy. Studies irrespective of their language were selected by two reviewers independently.

**Data extraction and synthesis:** Data extraction from the selected studies and risk of bias assessments were performed by two reviewers independently. Specific risk of bias tools were used according to the pertinent research designs of the included studies. Criteria for conducting a meta-analysis were not met and a qualitative synthesis was conducted.

**Results:** Twenty-nine studies fulfilled the eligibility criteria; that is, 11 RCTs, four prospective cohort studies, one retrospective cohort study and 13 cross-sectional studies. The quality of the evidence was low for most of the studies included in this review. Contrary to the general consensus, two RCTs, one prospective cohort study and two cross-sectional studies identified poorer periodontal health in patients with fixed orthodontic retainers.

**Conclusions:** The authors of this systematic review concluded that fixed orthodontic retainers in the majority of the 29 included studies seemed to be a method of retention that is rather compatible with periodontal health, or at least not related to severe detrimental consequences for the periodontium. No recommendations on the best type of fixed retainer to use could be given. High-quality evidence from long-term studies is necessary to provide definitive conclusions on the relationship between fixed retainers and periodontal health.

## Practice Point

- This review concluded that fixed orthodontic retainers in the majority of the 29 included studies seemed rather compatible with periodontal health or are at least not related to severe detrimental outcomes of the periodontium. No recommendation on the best type of fixed retainer to use in clinical practice could be given.
- The findings of this review should be considered in the context that: (1) five of the included studies reported poorer periodontal health around fixed retainers; (2) most included studies were of low quality; and (3) a variety of additional limitations identified in this critical appraisal could have skewed these results.
- Evidence from high-quality long-term studies is necessary to provide definitive conclusions on the relationship between fixed orthodontic retainers and periodontal health.

## Commentary



*Objectives and key findings of the systematic review*

Arn et al.[1] defined the following objectives for their systematic review: 1) 'to evaluate the potentially deleterious effects of fixed orthodontic retainers on periodontal health'; and 2) 'to compare different kinds of fixed retainers according to their effects on periodontal health, and if possible, to recommend [one] of them'. The majority of the 29 included studies found that orthodontic fixed retainers seemed rather compatible with periodontal health, but five studies reported poorer periodontal status in the presence of these retainers. The quality of evidence for most of these studies was low. No recommendations on the best type of fixed retainer to use in practice could be given.

*Methods of our critical appraisal of the systematic review*

We applied a three-step critical appraisal strategy for the systematic review. We assessed: 1) how the review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist;[2,3,4] 2) the methodological validity, by applying the AMSTAR 2 tool;[5] and 3) the risk of bias in the review using the ROBIS tool.[6,7] These assessments were conducted independently by two reviewers (PS and RMR) and disagreements were resolved through discussions between these operators. We adopted methods of the AMSTAR 2 tool to create an overall quality score.[5] Seven critical domains (Q1, Q2, Q4, Q8, Q9, Q13, Q14) were assigned for this purpose.

*Findings of our critical appraisal*

The findings of our critical appraisals are presented in Tables 1, 2 and 3. The overall quality of the review of the AMSTAR 2 assessment was rated as 'moderate' because we identified one unclear critical domain (partial yes) and two non-critical flaws. Table 4 summarises the

limitations identified in Tables 1, 2 and 3, and includes additional shortcomings. Of the ten limitations, two were assigned to the methods and eight to the reporting of the review. The limitations and strengths of this review are further explained below.

**Table 1 PRISMA checklist scores for the systematic review by Arn et al.[1]**

| Item | # | Reporting score* |
|---|---|---|
| Title | | |
| Title | 1 | Reported |
| Abstract | | |
| Structured summary | 2 | Reported |
| Introduction | | |
| Rationale | 3 | Reported |
| Objectives | 4 | Partially reported |
| Methods | | |
| Protocol and registration | 5 | Reported |
| Eligibility criteria | 6 | Reported |
| Information sources | 7 | Reported |
| Search | 8 | Reported |
| Study selection | 9 | Reported |
| Data collection process | 10 | Reported |
| Data items | 11 | Reported |
| Risk of bias in individual studies | 12 | Reported |
| Summary measures | 13 | Reported |
| Synthesis of results | 14 | Reported |
| Risk of bias across studies | 15 | Reported |
| Additional analyses | 16 | Not applicable |
| Results | | |
| Study selection | 17 | Partially reported |
| Study characteristics | 18 | Reported |
| Risk of bias within studies | 19 | Reported |
| Results of individual studies | 20 | Reported |
| Synthesis of results | 21 | Reported |
| Risk of bias across studies | 22 | Reported |
| Additional analysis | 23 | Not applicable |
| Discussion | | |
| Summary of evidence | 24 | Reported |
| Limitations | 25 | Reported |
| Conclusions | 26 | Reported |
| Funding | | |
| Funding | 27 | Not reported |

*Each PRISMA checklist item was scored as either: 1) reported; 2) not reported; 3) partially reported; 4) not applicable4

**Table 2 AMSTAR 2 scores for the systematic review by Arn et al.[1]**

| AMSTAR questions | Scores |
|---|---|
| Q1. Did the research questions and inclusion criteria for the review include the components of PICO? | Yes |
| Q2. Did the report of the review contain an explicit statement that the review methods were established before the conduct of the review and did the report justify any significant deviations from the protocol? | Partial yes |
| Q3. Did the review authors explain their selection of the study designs for inclusion in the review? | Yes |
| Q4. Did the review authors use a comprehensive literature search strategy? | Yes |
| Q5. Did the review authors perform study selection in duplicate? | Yes |
| Q6. Did the review authors perform data extraction in duplicate? | Yes |
| Q7. Did the review authors provide a list of excluded studies and justify the exclusions? | No |
| Q8. Did the review authors describe the included studies in adequate detail? | Yes |
| Q9. For RCTs* | |
| Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? | Yes |
| Q9. For NRSI** | |
| Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? | Yes |
| Q10. Did the review authors report on the sources of funding for the studies included in the review? | Yes |
| Q11. For RCTs* | |
| If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results? | No meta-analysis conducted |
| Q11. For NRSI** | |
| If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results? | No meta-analysis conducted |
| Q12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis? | No meta-analysis conducted |
| Q13. Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review? | Yes |
| Q14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? | Yes |
| Q15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review? | No meta-analysis conducted |
| Q16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review? | No |

* RCTs: randomised controlled trials
**NRSI: non-randomised studies of interventions

**Table 3 Tabular presentation for ROBIS results for the systematic review by Arn et al.[1]**

| Phase 1: Assessing relevance | Phase 2: Identifying concerns with the review process | | | | Phase 3: Judging risk of bias |
|---|---|---|---|---|---|
| Does the question addressed by the review match the target question? | Domain 1. Study eligibility criteria | Domain 2. Identification and selection of studies | Domain 3. Data collection and study appraisal | Domain 4. Synthesis and findings | Risk of bias in the review |
| Not applicable, because we did not formulate a target question | ☺ | ☺ | ☺ | ☺ | ☺ |

☺ = low risk of bias

**Table 4 Limitations of the methods and the reporting in the review by Arn et al.[1]**

| Limitation # | Item | Limitation |
|---|---|---|
| 1 | Registration or publication of the protocol | No publication or registration of a protocol a priori |
| 2 | Defining objectives | The Patients, Interventions, Comparators, Outcomes, Settings (PICOS) elements were not implemented in the objectives |
| 3 | Pilot testing of research methods | Not reported whether research methods such as study selection, data extraction, and bias assessments were pilot tested |
| 4 | Search strategy | Not reported whether an information specialist for the health sciences was consulted for the development of the search strategies |
| 5 | Information sources | Not reported in which information sources the reviewers had found the included studies |
| 6 | Excluded studies | A list of excluded studies with justifications for exclusion was not given |
| 7 | Contacting of authors | The reviewers reported that they would contact authors on missing or unclear data, but did not report on contacting authors on study eligibility or unclear items for the risk of bias assessment |
| 8 | Differences between the protocol and the review | Differences between the protocol and the review were not reported |
| 9 | Repository | It was not reported whether a repository (with name) was used to deposit data extraction forms, raw data etc |
| 10 | Funding of the systematic review | Funding sources and the role of the funder for this systematic review were not given |

*Limitations of the methods of the review*

Limitations of the methods were: (1) the protocol was not registered, for example, in PROSPERO[8] or published a priori which could have introduced risk of bias related to selective reporting of outcomes;[9,10,11] (2) the research objectives were defined, but should have been formulated using the Patients, Interventions, Comparators, Outcomes, Settings (PICOS) acronym. Using this format is important for the development of the search strategy[12] and for future reviewers who want to assess the reproducibility of this review or update it.

*Limitations of the reporting of the review*

The following eight items were not reported in the review: (1) pilot testing of the research methods. These procedures are important to fine-tune these methods a priori and to calibrate reviewers; (2) whether an information specialist for the health sciences was consulted for the development of the various search strategies; (3) the information source in which each included study was found. For example, end users of systematic reviews want to know which included studies were retrieved in the grey literature; (4) the references of excluded studies with justifications; (5) contacting of authors regarding eligibility of studies and unclear risk of bias issues; (6) differences between the review and the protocol; (7) whether a data repository was used for the deposition of for example: data extraction forms with definitions of variables, lists of excluded studies with rationale, raw data on the scoring of risk of bias with rationale, information on selective reporting within studies etc; and (8) the reviewers reported to have no potential conflicts of interest, but the sources of funding and the role of the funder of this review were not reported.

Not reporting on these items could jeopardise the trust in the outcomes of this review and could compromise its reproducibility. However, not reporting on these eight items does not necessarily imply that some of these reporting issues were not implemented. Contacting the reviewers would be the ideal strategy to verify the status on these reporting items.

*Strengths of the review*

This systematic review has important strengths: (1) it addressed a research question with a wide external validity, because a broad spectrum of orthodontic patients receives fixed orthodontic retainers; (2) mostly high-quality methodology was implemented; (3) an overall low risk of bias of the review process was assigned using the ROBIS tool; (4) up-to-dateness of the search; and (5) a solid assessment of the strengths and limitations of the review.

*Limitations of the included studies*

Three limitations of the included studies were identified; (1) most of them were of low quality; (2) a high diversity of patients, interventions, comparators, and outcomes complicated data synthesis; and (3) all were published studies. This latter issue could have skewed the findings of this systematic review, because research has shown that adverse effects of interventions are more frequently reported and are more severe in unpublished

versus published studies.[13,14] The reviewers correctly searched various sources of grey literature, but did not identify non-published research. Searching a broader spectrum of grey literature for reviews that assess the adverse effects of interventions could be indicated.

*Can we implement the findings of this review in daily practice?*

The reviewers concluded that the overall consensus of the included studies was that orthodontic fixed retainers seemed rather compatible with periodontal health. However, before implementing these findings in daily practice clinicians should: (1) consider that five of the 29 included studies reported contrary findings; (2) consider that most studies provided low-quality evidence; (3) assess whether the strengths of the review outweigh its limitations; (4) consider all patient-important outcomes regarding retention interventions; (5) weigh the costs of the intervention; and (6) assess whether the patients in the included studies differ from those in front of them.

*Conclusions*

This review addressed research questions on the adverse effects of fixed orthodontic retainers that are important for clinicians, researchers, policy makers, and a broad spectrum of orthodontic patients. The reviewers concluded that fixed orthodontic retainers in the majority of included studies seemed rather compatible with periodontal health or are at least not related to severe detrimental outcomes for the periodontium. No recommendation could be given on the best type of fixed retainer to use in clinical practice. The findings of this review should be considered in the context that: (1) five of the 29 included studies reported poorer periodontal health around fixed retainers; (2) most included studies were of low quality; and (3) various additional limitations identified in this critical appraisal could have skewed these results.



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Evidence-Based Dentistry (2020) **21**, 146-149. https://doi.org/ 10.1038/s41432-020-0144-0

# CHAPTER 7

## Which orthodontic retention protocol should I implement? A critical assessment of a randomized controlled trial

This is a non-edited version of the manuscript:

Steegmans PAJ, Cavagnetto D, Meursinge Reynders RA. Which orthodontic retention protocol should I implement? A critical assessment of a randomized controlled trial. Evid Based Dent. 2022 Dec;23(4):162-165.

## A commentary on

**Krämer A, Sjöström M, Apelthun C, Hallman M, Feldmann I.** Post-treatment stability after 5 years of retention with vacuum-formed and bonded retainers-a randomized controlled trial. Eur J Orthod 2022; DOI: 10.1093/ejo/cjac043**.**

## Abstract

**Trial design:** A single-centre two-arm parallel group randomised controlled trial.

**Objectives:** To assess differences in dental stability, patient perceptions and compliance and retainer failures in adolescents treated with vacuum-formed retainers (VFR) compared with those receiving bonded canine-to canine retainers after five years in retention.

**Methods:** In total, 104 eligible adolescents treated with fixed appliances in both jaws in a Swedish orthodontic clinic were randomised to two retention protocols. The intervention protocol consisted of a VFR covering all erupted teeth in the maxilla and a VFR in the mandible covering first premolar to first premolar. The controls received a VFR in the maxilla covering all erupted teeth and a bonded retainer wire to the lingual surfaces of the canines. The primary outcomes were various dental stability measures assessed at: debond (T1); six months (T2); 18 months (T3); and after five years (T4) in retention. Generalised estimating equations were used to quantify the effect of the different interventions on these outcome measures. One operator assessed all outcomes and participants could not be blinded. For the secondary outcomes, the perception and compliance with the retention protocols were assessed and the prevalence and rationale of retainer failure at T4. The trial was registered at ClinicalTrials.gov (NCT03070444) and the research project was supported by the Centre for Research and Development, Region Gävleborg, Sweden.

**Results**: Of the 104 randomised patients, 30 were not available at T4, leaving 35 patients in the intervention and 39 in the comparator group. An intention-to-treat analysis was used to impute outcomes for the missing patients. Post-treatment changes at T4 were small in both jaws. In the maxilla, the Little's Irregularity Index (LII) increased similar in both retention groups (median difference: 0.3 mm). In the mandible, the median difference for the LLI in the bonded retainer group was 0.1 mm compared with 0.6 mm in VFR group. In both retention protocols, the overjet remained stable, the overbite increased and the arch lengths continued to decrease. Intercanine and intermolar width remained stable in the mandible. Intermolar width decreased significantly in the maxilla. No differences in satisfaction were found between retention protocols after five years. Also, 72% of patients had stopped or rarely wore the VFR appliances at T4. Besides some retainer failures in both groups, no serious adverse effects associated with the retainers were reported.

**Conclusions:** Most post-treatment changes in both retention protocols were small in both jaws, except for the anterior alignment in the mandible, which was more stable in the bonded retainer group. This difference is possibly not related to the retention technique but to the poor compliance with the VFRs and the inclusion of adolescents only. Satisfaction with both protocols was similar.

## Practice Point

- At five years in retention, most post-treatment changes were small in both jaws for both retention protocols, except for the anterior alignment in the mandible, which was more stable in the bonded retainer group.
- The differences in the results are possibly not related to the appliances used, but to the poor compliance identified in the removable retainer group and to the inclusion of adolescents only, which tend to adhere less to wearing removable retainers compared with adults. The satisfaction with both retention protocols was similar.
- Before implementing the findings of this RCT in clinical practice, one should consider the high risk of bias in the results and additional limitations presented in Tables 4 and 5.

## Commentary

*Research questions*

In this commentary we appraised a randomised controlled trial (RCT) by Krämer et al.[1] that assessed the following primary research question: 'in adolescent patients treated with fixed orthodontic appliances in the maxilla and mandible, how do post-treatment changes compare between two different retention protocols at debond (T1), after six months (T2), after 18 months (T3) and after five years (T4)'. The retention protocol in the intervention group was a vacuum-formed retainer (VFR) in the maxilla and mandible. The retention protocol in the comparator group was a VFR in the maxilla and a bonded retainer wire to lingual surfaces of the canines only. A secondary question was: 'what was the patient's perception and compliance regarding the different retention protocols and what was the prevalence and rationale of retainer failure after five years of retention?'. The elements 'participants', 'interventions', 'comparators', 'outcomes', 'time points', 'setting' of the PICOTS acronym of this RCT are reported in Table 1.

| Table 1 The PICOTS elements | |
|---|---|
| **Items** | **Description** |
| Participants | • Adolescent patients treated with fixed orthodontic appliances |
| Interventions | • VFR covering all erupted teeth in the maxilla and a VFR in the mandible covering first premolar to first premolar. VFR wear was gradually decreased to 1–2 nights per week only after two years of retention and on |
| Comparators | • VFR in the maxilla covering all erupted teeth and a bonded retainer wire to the lingual surface of the canines. VFR wear was gradually decreased to 1–2 nights per week only after two years of retention and on. The mandibular retainer was not removed during the full retention period |
| Outcomes | • Primary outcomes: post-treatment dental and arch stability measures in the maxilla and mandible |
| | • Secondary outcomes: patient's perception and compliance regarding the different retention protocols and the prevalence and rationale of retainer failure |
| Time points | • Primary outcome: start of retention (T1), 6 months (T2), 18 months (T3), and after five years in retention (T4)<br>• Secondary outcomes: after five years in retention |
| Setting | • Orthodontic clinic in Gävle, public dental health service, Region Gävleborg, Sweden |

*Methods of the RCT*

A total of 165 patients were eligible, of which 61 declined to participate in the trial. The remaining 104 eligible patients were then randomised to 52 patients in the intervention and 52 in the comparator arm. Digitised models were used to assess the stability of the dentition at the start of retention (T1), at six months (T2), at 18 months (T3), and after five years in retention (T4). Questionnaires were used to assess the perception and compliance with the retention protocols at T4. The prevalence and rationale of retainer failure after five years of retention was also measured. Treatment with fixed appliances was conducted by different orthodontists but all retention appliances were placed and outcomes were assessed by one orthodontist (the first author) during the entire five-year retention period.

*Results of the RCT*

At five years in retention, 30 of the 104 randomised patients were not available for outcome assessment, leaving, respectively, 35 patients in the intervention and 39 in the comparator group. An intention-to-treat analysis was implemented, which gave 50 patients in the intervention and 51 in the control group. Post-treatment changes at T4 in both retention protocols were small in both jaws. In the maxilla, the Little's Irregularity Index (LII) increased similarly in both retention groups (median difference: 0.3 mm). In the mandible, the median difference for the LLI in the bonded retainer group was 0.1 mm compared with 0.6 mm in VFR group. In both retention protocols, the overjet remained stable, the overbite increased and the arch lengths continued to decrease. Intercanine and intermolar width remained stable in the mandible. Intermolar width decreased significantly in the maxilla. At T4, patients were very satisfied with both the outcomes of treatment and the assigned retention protocol. No differences in satisfaction were found between the retention protocols. Besides

some retainer failures in both groups, no serious adverse effects associated with the retainers were reported.

*Methods for the critical appraisal*

The checklist of the CONSORT statement[2] was used to assess how this RCT was reported and the risk of bias 2 (RoB2) tool[3] was used to assess the risk of bias. All items in these tools were completed independently by two operators (PS and DC). The third operator (RMR) was consulted in the case of disagreements between these operators. Shortcomings that were not covered by these tools were also reported. All three authors developed and drafted this commentary and approved the final version of this manuscript.

*Results of the critical appraisal*

Our assessment of the reporting items according to the CONSORT statement[2] were reported in Table 2. In this table, we only list the items that were either 'not' or 'partially reported'. The results of the risk of bias assessment with the RoB2 tool[3] are presented in Table 3 for each outcome separately. The limitations reported by the authors of the RCT are given in Table 4. All limitations identified with the CONSORT checklist[2], the RoB2 tool[3] and additional limitations identified during our critical appraisal of this RCT are explained and summarised in Table 5.

**Table 2 Items not reported according to the CONSORT statement[2]**

| CONSORT item | Type of reporting |
|---|---|
| 1b. Structured summary of trial design, methods, results and conclusions | Partially reported |
| 3b. Changes in the eligibility criteria compared with the protocol | Not reported |
| 6b. Changes in the trial outcomes compared with the protocol | Not reported |
| 16. Secondary outcome numbers analysed | Partially reported |
| 19. Harms | Partially reported |
| 20. Limitations | Partially reported |
| 21. Generalisability of the trial findings | Not reported |

**Table 3 Risk of bias domains for each outcome[1]**

| Outcome | D1 | D2 | D3 | D4 | D5 | Overall |
|---|---|---|---|---|---|---|
| Outcome 1 | Low risk of bias | High risk of bias | Some concerns | High risk of bias | High risk of bias | High risk of bias |
| Outcome 2 | Low risk of bias | High risk of bias | Some concerns | Low risk of bias | High risk of bias | High risk of bias |
| Outcome 3 | Low risk of bias | High risk of bias | Some concerns | Low risk of bias | High risk of bias | High risk of bias |
| Outcome 4 | Low risk of bias | High risk of bias | Some concerns | High risk of bias | High risk of bias | High risk of bias |

Note:
Outcome 1: differences in post-treatment changes in the maxilla and mandible between two retention protocols
Outcome 2: differences in patient's satisfaction between two retention protocols
Outcome 3: prevalence of compliance with wearing the VFR
Outcome 4: prevalence of retention failure in the different retention groups
Domain 1: bias arising from the randomisation process
Domain 2: bias due to deviations from the intended intervention
Domain 3: bias due to missing outcome data
Domain 4: bias in measurement of the outcome
Domain 5: bias in selection of the reported result

**Table 4 Summary of the limitations identified by the authors of the RCT**

| Limitations reported by the authors | Description |
|---|---|
| Blinding issues | Complete blinding was not possible because of the type of interventions |
| Little's Irregularity Index | The limitations of Little's Irregularity Index, such as not considering spacing or ro-tations with intact contact points |
| Selection bias | Selection bias because patients who declined to participate in the trial could have been the poor compliers with the retention protocols |
| Compliance issues | Differences in results are possibly not related to the retention technique but to the quality of compliance. Good compliance was required in the VFR group and no compliance in the fixed retainer group |
| Hawthorne effect | False-positive bias because of the awareness of the participants being observed |
| Duration of the trial | The long duration (five years) of the trial might have influenced compliance |

**Table 5 Additional limitations identified during the critical appraisal of the RCT**

| Additional limitations identified during the critical appraisal | Description |
|---|---|
| Misleading reporting related spin in the abstract[4] | The poor compliance with the VFR was not reported in the abstract, which could mislead the reader |
| Differences in the lengths of the retention devices | In the intervention group the VFR in the mandibular arch covered eight teeth, that is, first premolar to first premolar, while the comparator group had a shorter length covering only 6 teeth, that is, from canine to canine |
| Deviations from the planned protocol | • Differences between the two protocols (2009 and 2017) and with the final study were not reported nor the rationale for these changes. Deviations from the planned protocol refer to:<br>• The eligibility criteria of the 2017 protocol refer to child, adult and older adult. In the final RCT only adolescents were included<br>• Compliance and retainer failures were not defined as outcomes in the 2017 protocol<br>• The 2009 protocol planned to assess secondary outcomes at four time points and not just at five years in retention as was reported in the final RCT<br>• Primary outcomes were measured on digital models and not on dental casts as planned in the 2009 protocol<br>• The assessment of outcomes on adverse effects were not planned in the protocols, but in the final RCT the authors reported on adverse effects |
| Poor reporting on the definitions of secondary outcomes | Definitions of secondary outcomes such as satisfaction, retainer failure etc were not reported |
| Poor reporting on adverse effects | In the final RCT, the authors reported that no serious adverse effects associated with the retainers were observed, but did not report which adverse effects were assessed, for example, no information was given regarding caries and periodontal problems |
| Unreliable sample size calculation | The sample size calculation was not planned a priori and was based on an arbitrary value |
| Incomplete reporting on the selection procedures of patients | It was not reported who selected the patients (preferably done by two operators) and how many patients were assessed for eligibility and how many of these patients did not meet the inclusion criteria and why they were excluded. The authors reported only the number of eligible patients |
| Bias in measurement of the outcome | Outcomes were assessed by one outcome assessor only, who also placed all retainers and conducted all follow-up procedures |
| Bias due to deviations from the intended intervention | Many patients (72%) had already stopped wearing the VFRs at the last follow-up, due to unknown reasons, which implies poor adherence to the intervention |
| Lost to follow up | High prevalence of patients, that is, 29% (30/104), were lost to follow-up |
| Caution regarding the generalisability of the trial findings | Generalisability of the trial findings should be done with caution, because:<br>• Only adolescents were included. This implies that this study cannot be generalised to adults, because adults possibly comply differently with VFRs<br>• Selection bias<br>• The incomplete reporting on the selection procedures of patients |
| Raw data | Raw data were not given as additional files or in a repository and could only be obtained on 'reasonable request to the corresponding author' |

Note: additional limitations refer to the shortcomings identified with the CONSORT checklist,[2] the RoB 2 tool[3] and those limitations identified during our critical appraisal, which were not already reported by the authors of the RCT.

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*Ethics declaration*

*The authors declare no conflicts of interest.*



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# CHAPTER 8

## Fixed flexible spiral wire retainers and unwanted tooth movements: a Case Report

This is a non-edited version of the manuscript:

Steegmans PAJ, Jonkman REG, de Lange J. Fixed Flexible Spiral Wire Retainers and Unwanted Tooth movements: A Case Report. Appl. Sci. 2023, 13(2), 922.

## Abstract

This case report presents a study of unwanted tooth movements during the retention phase after orthodontic treatment. The early recognition of these unwanted tooth movements is paramount for patients and clinicians to prevent the associated negative consequences. A 21-year-old male presented with aesthetic complaints regarding his upper front teeth. He underwent orthodontic treatment at the age of 9 years and 11 months and finished his treatment 2 years and 11 months later. Flexible spiral wires (FSW) were bonded to the anterior segment of the upper and lower jaws to stabilize the end result. The failure of the fixed retainers had never occurred previously. The diagnostic assessment demonstrated a previously orthodontically treated class I malocclusion with excessive angulation and torque differences in the maxillary anterior segment. To correct the position of the maxillary anterior segment and prevent further misalignment, the patient received orthodontic re-treatment. Thereafter, the result was retained with fixed braided-rectangular-wire (BRW) retainers located at 12–22 and 33–43 and a vacuum-formed retainer (VFR) in the maxilla. The end result appeared to be stable after 28 months of retention. Unwanted tooth movements can occur during the orthodontic retention phase and might result from the use of fixed flexible spiral wire retainers. Follow-up appointments are recommended to monitor the stability and recognize these movements.

**Keywords:** orthodontics; dentistry; adverse effects; stability; fixed retainers; retention; unwanted tooth movements

## 1.Introduction

The retention phase of an orthodontic treatment aims to maintain the end result of orthodontic treatment and is of great importance for both patients and orthodontists. In 1934, Oppenheim stated: “Retention is one of the most difficult problems in orthodontia; in fact, it is the problem” [1]. Without retention, teeth have the possibility of (1) returning to their initial position, also known as ‘relapse’ [2], or (2) displacement as a result of growth and aging [3]. Orthodontic retention can be performed in two ways: (1) by placing fixed or removable appliances on the teeth or (2) by additional treatments of the teeth and periodontal structures in order to achieve stability. Fixed retainers are usually bonded to the palatal or lingual side of the anterior teeth [4]. Hawley or vacuum-formed retainers (VFR) can be taken off by the patient. Additional treatments used to prevent relapse are (1) small surgical procedures that cut the supra-crestal periodontal fibers around the teeth to reduce the chance of relapse [5] or (2) interproximal enamel reduction of the lower front teeth to create space for the corrected crowding and to compensate in advance for the expected reduction in the inter-canine width during aging [6].

Currently, fixed retention is commonly used in orthodontic practice [7,8]. Previous research on the long-term outcomes showed that when using a flexible spiral wire (FSW) retainer bonded to the mandibular anterior segment, the alignment is stabilized in 90.5% (200/221) of cases after 5 years of retention [9]. However, these fixed retention appliances may also fail or have adverse effects. Recently, a systematic review was conducted to evaluate the available evidence on the failure of fixed retainers and reported that fixed retainers fail in a range of 7.3% to 50%, according to which detachment at the adhesive–enamel interface was the most commonly reported type of failure [10]. Other observed adverse effects of fixed retainers in the orthodontic literature are detachment at the adhesive–wire interface [11], wire fracture [12], wire untwisting [13], and calculus accumulation [14,15]. Wire untwisting may lead to unwanted changes in the tooth position and can be associated with the development of gingival recessions [13,16,17]. Other causes of unwanted tooth movements can be tongue thrust or personal habits [18,19]. A clinical case of unwanted tooth movements during the retention phase is presented in this case report. This case showed that the unwanted tooth movement was the direct result of an untwisting FSW, because the maxillary teeth were displaced in a different direction from the original tooth position (Figure 1), which clearly showed that this was not a case of simple relapse. The early recognition of these unwanted tooth movements is paramount for patients and clinicians to prevent the associated negative consequences [20].

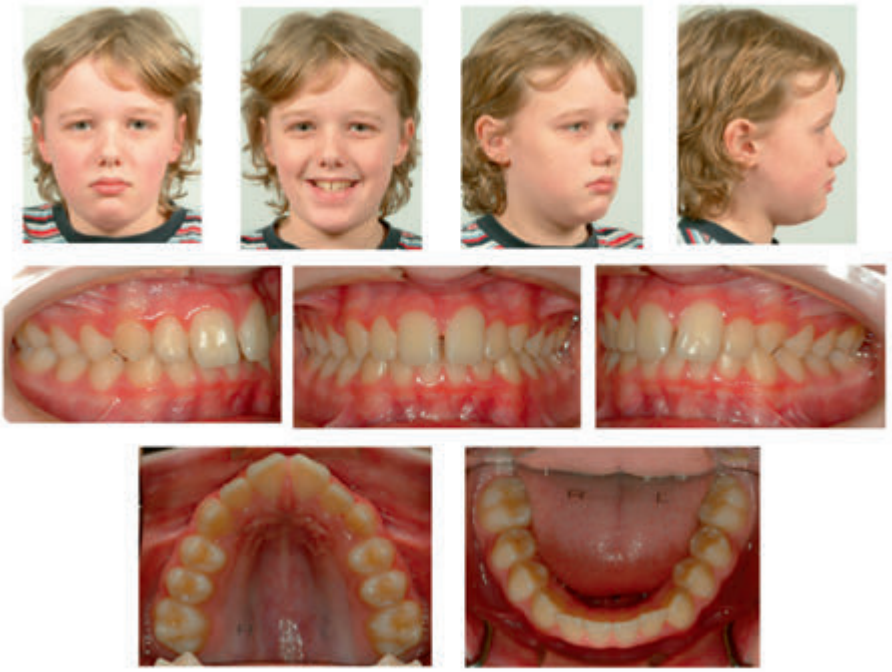


**Figure 1.** Extra-oral and intra-oral photographs before first orthodontic treatment.

## 2. Materials and Methods

This case was reported according to the Case Report (CARE) guidelines [21]. The CARE checklist of items used for this case report is presented in Supplementary File S1.

**Patient information**

A 21-year-old Caucasian male presented with aesthetic complaints regarding his upper front teeth. He previously underwent orthodontic treatment for a deep bite at the age of 9 years and 11 months for 2 years and 11 months. He was treated with high-pull headgear (Headgear, Dentsply GAC International, NY, USA) followed by full fixed appliances (3M Victory Series APC conventional twin brackets, 3M Health Care Division, London, Canada), and flexible spiral wires (0.0195-inch, 3-strand, heat-treated twist wire, Wildcat, GAC International, Bohemia, NY, USA) were bonded to all the anterior teeth between 13–23 and 33–43 to stabilize the end result (Figure 2). Over the last few years (the moment of onset was unknown), he noted a continuing shift in the position of his upper front teeth (Figure 3A). Aside from his aesthetic complaints, he was concerned that the situation would deteriorate. With regard to his medical history, he only used antihistamines for hay fever if necessary. There was no record of dental trauma, and he was unfamiliar with oral parafunctions. The failure of the fixed retainers had never occurred, and he did not experience any pain or functional constraints.

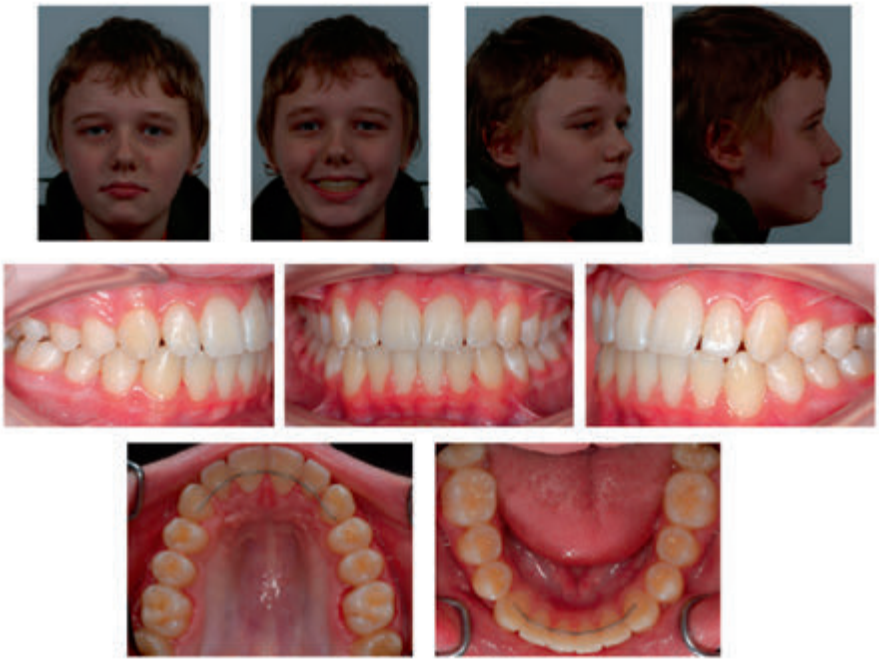
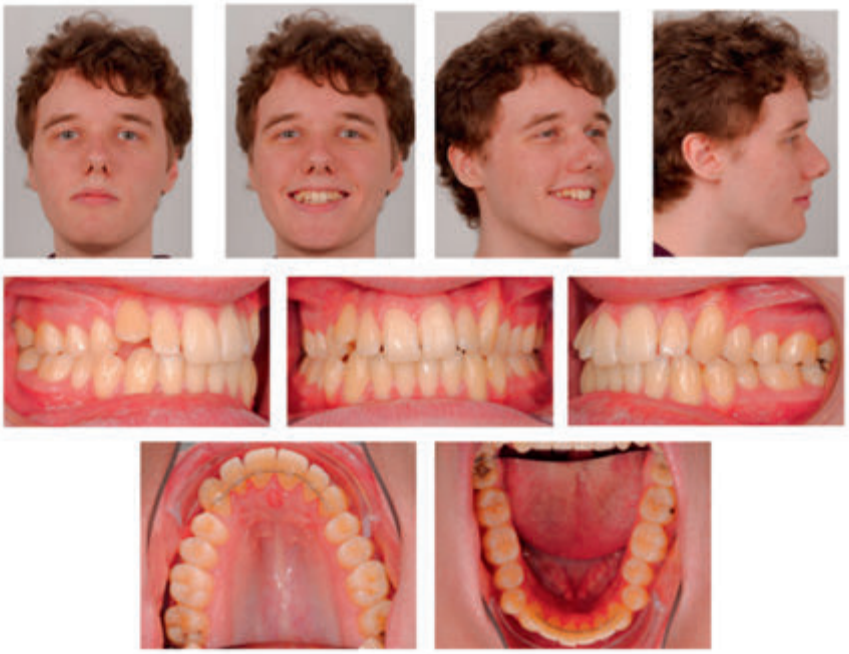
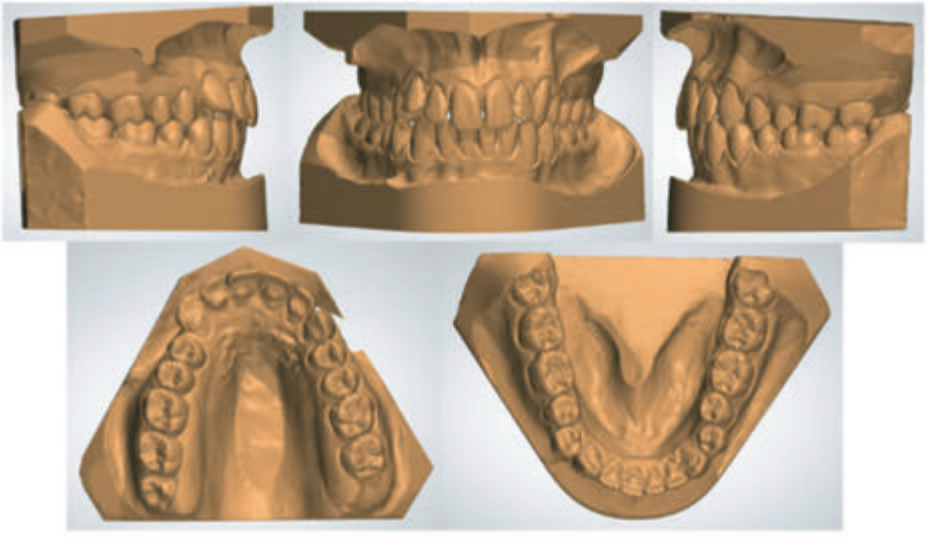


**Figure 2.** Extra-oral and intra-oral photographs after first orthodontic treatment.



(A)



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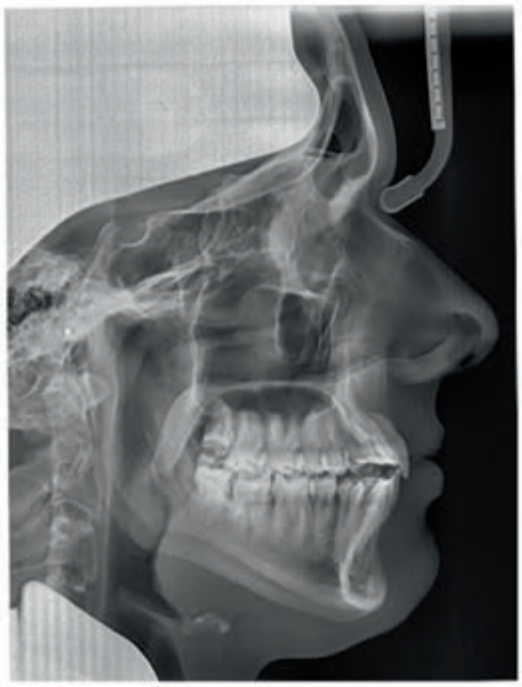
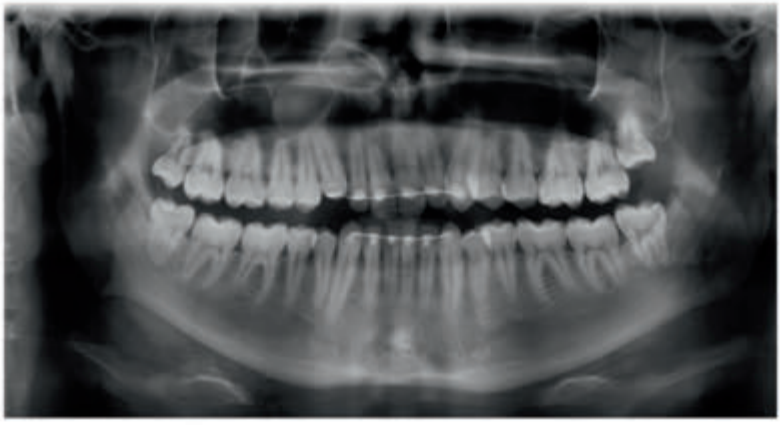


(C)



(D)

**Figure 3.** Documentation before orthodontic re-treatment. (**A**) Extra-oral and intra-oral photographs. (**B**) Dental casts. (**C**) Lateral cephalometric radiograph. (**D**) Panoramic radiograph.

**Clinical findings**

Figure 3A shows the case at the first presentation. The photographs demonstrate that the 13 shows excessive palatal root torque, and the 23 shows excessive buccal root torque. A cant of the upper incisors can be observed. Moreover, cross-bites are present between the 14 and the 44 and between the 23 and the 34.

**Timeline**

The timeline for this patient is presented in Supplementary File S2.

**Diagnostic Assessment**

The patient presented with a Class I profile and a chin point deviation to the right side (Figure 3A). The intra-oral assessment showed good oral hygiene, a thin gingival biotype, group function on the left and right side, and fixed retainers (0.0195-inch, 3-strand, heattreated twist wire, Wildcat, GAC International, Bohemia, NY, USA) in the upper anterior segment and lower anterior segment (Figure 3A). The dental cast assessment showed a Class I molar and canine occlusion, an overjet of 2 mm, and an overbite of 3 mm. A cant of the upper incisors was present with palatal root torque of the 13 and buccal root torque of the 23. Crossbites were present between the 14/44 and the 23/34. The arch length discrepancy measurement resulted in values of 0 mm in the case of the maxillary arch and −4 mm in the case of the mandibular arch. No tooth size discrepancy was present. The PAR index resulted in a score of 12 points [22] (Figure 3B). The lateral cephalometric radiograph showed a Class I intermaxillary relationship with an ANB angle of 3.2◦ (VistaPano S Ceph, Dürr Dental imaging software, Dürr Dental SE, Bietigheim-Bissingen, Germany) (Figure 3C). The panoramic radiograph (VistaPano S Ceph, Dürr Dental imaging software, Dürr Dental SE, Bietigheim-Bissingen, Germany) showed a maxillary sinus mucosal cyst (MSMC) on the right side and external apical root resorption located at the 12, 11, and 21 (Figure 3D).

**Diagnosis**

This clinical, radiographic, and dental cast examination contributed to the following orthodontic diagnosis: A 21-year-old male with an Angle Class I malocclusion, angulation, and torque differences in the maxillary anterior segment, with cross-bites located at 14/44 and 23/34, a thin gingival biotype, external apical root resorption located at 12, 11, and 21, and the presence of fixed retainers (0.0195-inch, 3-strand, heat-treated twist wire, Wildcat, GAC International, Bohemia, NY, USA) located between 13–23 and 33–43. 2.2.

**Prognosis**

The torque and angulation differences in the maxillary anterior segment were not observed before (Figure 1) or after the orthodontic treatment from 2006 to 2009 (Figure 2). From 2009 to 2017, no failure of the fixed retainers had occurred, and no oral parafunctions were present. It was hypothesized that the FSW retainer caused these unwanted tooth movements [9,16]. Since the patient identified a continued worsening of the position of the upper front teeth, it is likely that this process of unwanted tooth movement was persistent

and consequently resulted in a worse prognosis. For example, the development of gingival recessions may occur [17]. A recent case report showed a similar situation that resulted in the exposure of the apex of a canine [20]. A pilot study based on a retrospective data analysis showed that the removal of the FSW retainer led to the cessation of further unwanted tooth movement [23].

**Therapeutic intervention**

To correct the position of the maxillary anterior segment and prevent further misalignment, the patient received orthodontic re-treatment for 2 years and 4 months. The fixed FSWs (0.0195-inch, 3-strand, heat-treated twist wire, Wildcat, GAC International, Bohemia, NY, USA) in the maxilla and mandible were removed. Afterward, fixed appliances were placed (3M Victory Series APC conventional twin brackets, 3M Health Care Division, London, Canada). To correct the excessive palatal root torque of the 13, we incorporated the 13 into the fixed appliances with a 0.012-inch NiTi overlay wire (Sentalloy, Dentsply GAC international, Bohemia, NY, USA) on a 0.016 × 0.022-inch SS base wire (Stainless Steel Ideal® Form, Dentsply GAC international, Bohemia, NY, USA). In this way, the risk of unwanted reactionary tooth movements was reduced. During the active orthodontic treatment, a panoramic radiograph (VistaPano S, Dürr Dental imaging software, Dürr Dental SE, Bietigheim-Bissingen, Germany) was performed to monitor the root resorption observed in the maxillary anterior region in the initial stage of the treatment [24] (Figure 4). It appeared to be stable. However, it was difficult to reach a conclusion in this regard, since (1) a great difference in the tooth position between the two panoramic radiographs and (2) variations in quality between the panoramic radiographs were observed due to the use of different radiographic devices. The oral hygiene was checked at every orthodontic appointment. If necessary, instructions were given to maintain the quality of the patient's oral hygiene during the orthodontic treatment. After active orthodontic treatment over 2 years and 4 months, the treatment result was stabilized with fixed braided-rectangular-wire (BRW) retainers (Forestaflex, Forestadent®, Bernhard Förster GmbH, Pforzheim, Germany) located at 12–22 and 33–43. We opted for the BRW retainers, which achieve better torque control compared to flexible spiral wires (FSW) [25]. In addition, a VFR was prescribed for approximately 10 h a day to cover all the maxillary teeth. According to the current literature, the part-time wear of the VFR should be sufficient enough to generate stability [26]. Table 1 provides a detailed overview of the interventions.

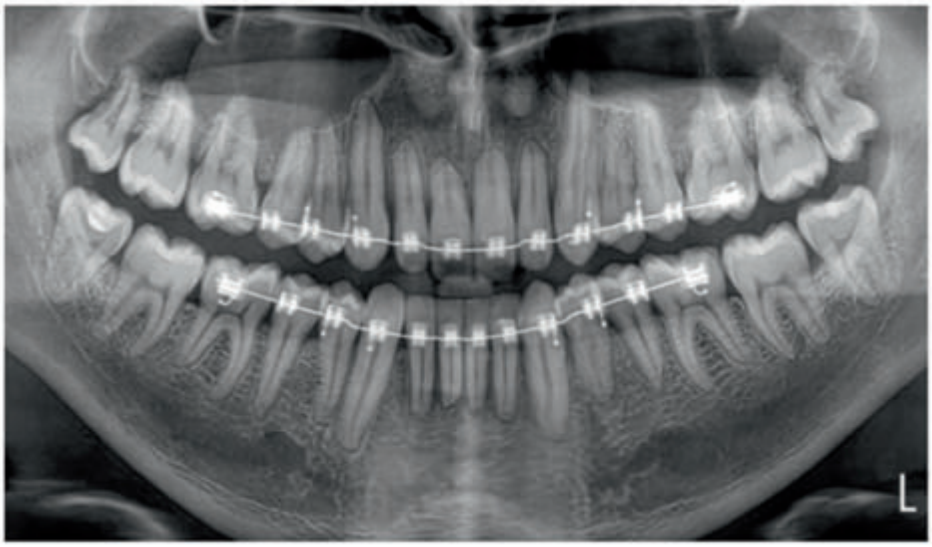



**Figure 4.** Panoramic radiograph during orthodontic treatment for monitoring root resorption.

**Table 1.** Interventions for the orthodontic re-treatment.

| Intervention | Description |
|---|---|
| Removal of the fixed flexible spiral wires | Maxilla: 0.0195-inch, 3-strand, heat-treated twist wire (Wildcat, GAC International, Bohemia, NY, USA) located on the palatal surface 13-12-11-21-22-23<br>Mandible: 0.0195-inch, 3-strand, heat-treated twist wire (Wildcat, GAC International, Bohemia, NY, USA) located on the lingual surface 33-32-31-41-42-43 |
| Fixed appliance therapy | Type: 3M Victory Series APC conventional twin brackets (3M Victory Series APC conventional twin brackets, 3M Health Care Division, London, Canada)<br>Prescription: MBT<br>Slot system: 0.022-inch<br>Wires: 0.012-inch NITI *, 0.014-inch NITI*, 0.016-inch NITI *, 0.018-inch NITI*, 0.016 × 0.022-inch NITI *, 0.017 × 0.025-inch NITI *, 0.016 × 0.022-inch SS **, 0.017 × 0.025-inch SS **<br>Overlay wires: 0.012-inch NITI *, 0.014-inch NITI *, 0.016-inch NITI *, 0.018-inch NITI * |
| Retention therapy | Maxilla: 0.016 X 0.016-inch, 8-stranded, braided rectangular wire (Forestaflex, Forestadent®, Bernhard Förster GmbH, Pforzheim, Germany) located on the palatal surface of 12-11-21-22 in combination with a vacuum-formed retainer<br>Mandible: 0.016 × 0.022-inch, 8-stranded, braided rectangular wire (Forestaflex, Forestadent®, Bernhard Förster GmbH, Pforzheim, Germany) located on the lingual surface of 33-32-31-41-42-43 |

*: Dentsply GAC Sentalloy® (Dentsply GAC international, Bohemia, NY, USA), **: Dentsply GAC Stainless Steel Ideal® Form (Dentsply GAC international, Bohemia, NY, USA).

## 3. Results

*3.1. Follow-Up and Outcomes*

3.1.1. Clinician- and Patient-Assessed Outcomes

The end result of the orthodontic re-treatment is shown in Figure 5. The cant of the upper incisors, the excessive palatal and buccal root torque of the 13 and 23, and the crossbites were corrected. In addition to aesthetic improvement, cuspid guidance on the left and right sides was achieved. However, the panoramic radiograph showed an increase in root resorption (Figure 4), and a buccal gingival recession was observed at the 23 (Figure 5). To assess the outcome of this orthodontic re-treatment, the Peer Assessment Rating (PAR) index was consulted and resulted in a PAR score of 2 [22]. Compared to the PAR score measured before the orthodontic re-treatment (PAR score of 12), the malocclusion improved by 83% (10/12). The patient participated in the ESAS patient satisfaction evaluation questionnaire to assess the outcome of the orthodontic retreatment. ESAS (EFOSA Self Assessment System) is a quality assessment system available to all orthodontists in Europe [27]. This patient satisfaction evaluation questionnaire rates different aspects of the treatment, e.g., patient satisfaction with the orthodontist, assistants, practice, and overall treatment. The completed questionnaire is provided (Supplementary File S3). The answers indicated that the patient was satisfied with nearly all aspects. Nevertheless, the treatment duration was slightly longer than expected, and he believed that the waiting room was not comfortable enough.

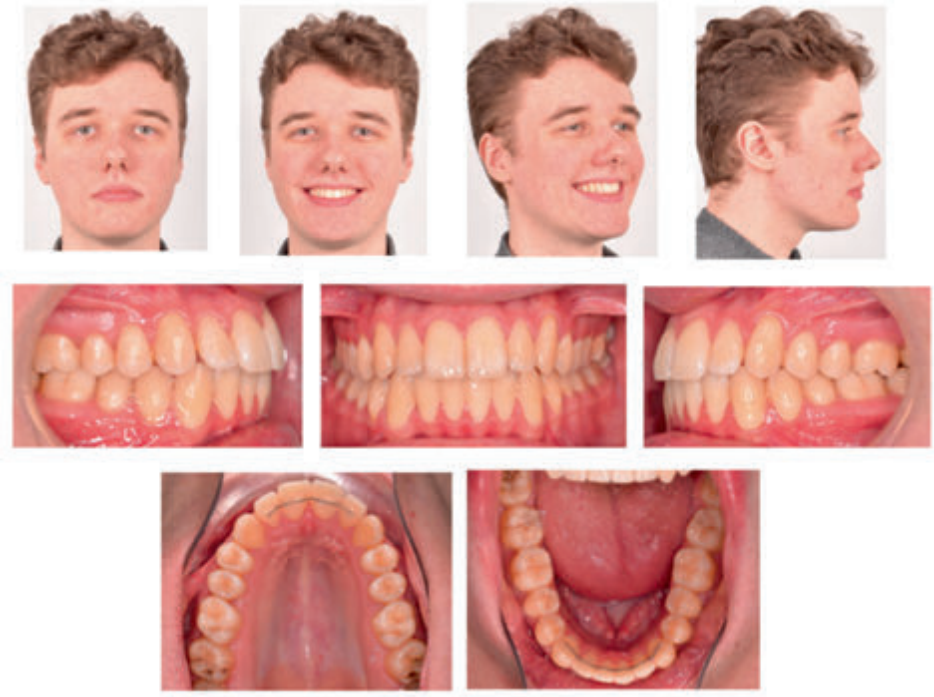


**Figure 5.** Extra-oral and intra-oral photographs after orthodontic re-treatment

### 3.1.2. Important Follow-Up Test Results

Since the patient went abroad for 3 years, the first follow-up appointment was scheduled for April 2022 (28 months after the end of the orthodontic re-treatment). At that moment, the bonded retainers were still fixed and had not been displaced. He still wore the VFR for approximately 10 h a day. An intra-oral examination showed a class I occlusion with an overjet of 2 mm and an overbite of 3 mm (Figure 6). These findings implied that the end result of the orthodontic re-treatment seemed to be stable. Unfortunately, the patient's oral hygiene was insufficient because, plaque and calculus were present around the fixed retainer in the mandibular anterior segment.

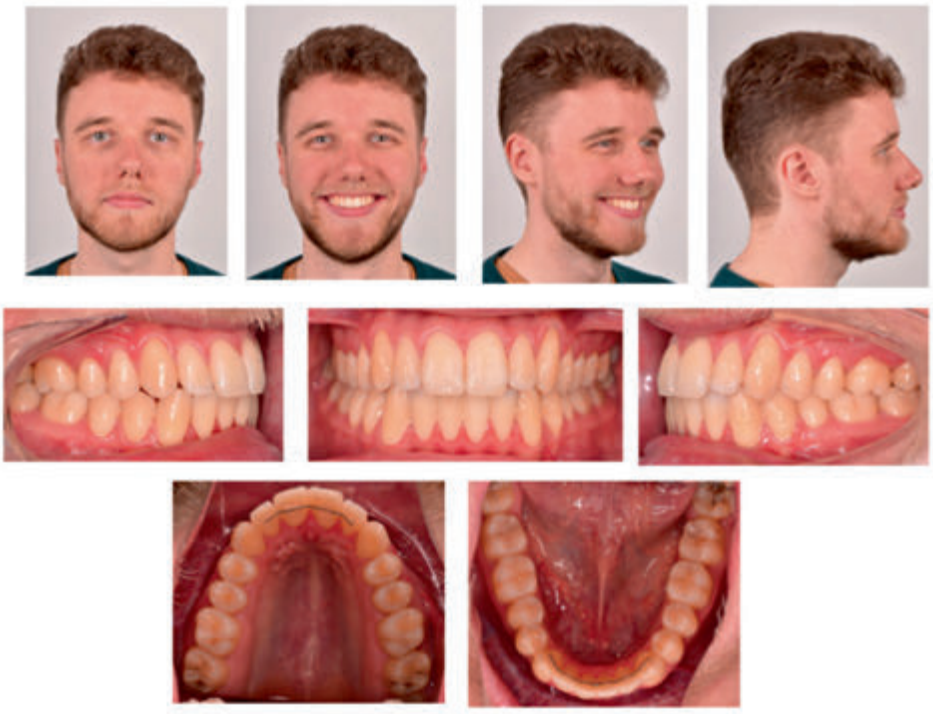


**Figure 6.** Extra-oral and intra-oral photographs 28 months after orthodontic re-treatment.

### 3.1.3 Intervention Adherence and Tolerability

The patient was compliant with the intervention. The oral hygiene was sufficient during the orthodontic treatment, and all the check-up appointments were undertaken. According to the patient, his aesthetic concerns and awareness of the need for orthodontic treatment could be attributed to this adherence.

3.1.4. Adverse and Unanticipated Events

During the active orthodontic re-treatment, an increase in root resorption occurred, and a buccal gingival recession was observed at the 23.

## 4. Discussion

This case report illustrates an adverse effect in orthodontics. This concerned unwanted tooth movement during the retention phase, probably due to the fixed retainer in the upper jaw. Even though fixed retainers are effective in preventing relapse, previous research has shown that fixed FSWs may also lead to unwanted effects and can complicate oral hygiene, with negative consequences for the periodontium [9,16,28–30]. Katsaros et al. described two possible effects of fixed FSWs during the retention phase: (1) the X-effect, a torque difference between two adjacent mandibular incisors, and (2) the twist-effect, an increase in the buccal inclination of the canine [16]. The X-effect or twist effect was observed in 2.7% (6/221) of the evaluated patients during a retention period of 5 years [9]. Recently, Singh described a case in which a combination of the X-effect and twist-effect was present, leading to the avulsion of the canine [20]. These reported 'twist-effects' are similar to the tooth movements described in this case report. However, in the current case report, the fixed FSW retainer was located in the upper jaw, while previous studies investigated fixed FSWs in the lower jaw [9,16,20,28]. It is hypothesized that the forces that contribute to the etiology of these unwanted tooth movements might be generated in three ways: (1) by the untwisting of the round flexible spiral wires (tooth movements generated by these forces might also be the reason for the observed root resorption localized at the 12, 11, and 21 on the panoramic radiograph from July 2017 (Figure 3D) [31]), (2) the mechanical deformation of the wire as a result of masticatory forces, and (3) the elastic deflection of the wire due to an inadequate passive bonding procedure [25]. One or more of the aforementioned etiologic factors might explain the situation described in this case report. To prevent a recurrence of these unwanted tooth movements, BRWs were bonded to the upper and lower jaws after the second orthodontic treatment. Fiber-reinforced composite or polyethylene splints could represent a viable alternative to conventional metallic bonded retention [32]. However, these materials have been shown to be less clinically reliable over time than stainless steel retainers [33]. A rectangular chain retainer could also have been a good alternative for the fixed retention in the upper and lower jaws. However, according to Arnold et al., BRWs achieve higher torque control [25]. Therefore, we chose to apply BRWs. Due to occlusal interferences with the lower canine, the retainer in the upper jaw was bonded to the incisors alone. However, it has been shown that significantly fewer rotational changes occur when fixed retainers are bonded from 13 to 23 compared to fixed retainers bonded from 12 to 22 [34]. Therefore, a VFR was prescribed to prevent rotational changes of the 13 and 23. According to a systematic review conducted by Bellini-Pereira et al., fixed retainers and VFRs in the upper jaw are equally effective in maintaining the end result of an orthodontic treatment (with a moderate level of certainty) [14]. Hence, a VFR placed in the upper jaw should stabilize the cuspids adequately. It has been shown that the failure of fixed orthodontic retainers occurs more frequently in the upper jaw compared to the lower jaw [10]. Therefore, if the fixed retainer fails from 12 to 22, the VFR will stabilize the alignment until the retainer can be repaired. The limitations of this case report include (1) the delay of the first follow-up appointment, which was eventually scheduled after 28 months due to the

patient's departure abroad and the COVID-19 pandemic. Fortunately, the fixed retainers did not fail in this period. However, the first follow-up appointment should have been scheduled earlier, since most failures of fixed retention occur in the first 6 months after the bonding of fixed retainers. In addition, failure is more frequent in the upper jaw [10]. (2) The existing root resorption should have been monitored earlier and more often during the active orthodontic re-treatment. (3) Moreover, case reports are considered to represent the lowest level of evidence. Implications for future research could include the design of studies with a long-term follow-up that assess variables that could influence the stability of fixed orthodontic retention, such as the periodontal and dental status of the patient, the type and dimensions of the retainer wire, the type and quantity of the composite used, and the placement technique.

## 5. Conclusions

In conclusion, fixed retainers appear to be effective in maintaining alignment after orthodontic treatment. However, unwanted tooth movements might result from the use of fixed flexible spiral wire retainers, requiring orthodontic re-treatment. Follow-up appointments are recommended to monitor the stability and to recognize unwanted tooth movements at an early stage. The results of this case report are of great importance for researchers, patients, and clinicians. In particular, dentists should be aware of these possible adverse effects of fixed flexible spiral wire retainers, since they regularly perform dental check-ups after orthodontic treatment. Therefore, dentists play an important role in recognizing these unwanted tooth movements.

**Supplementary Materials:** The following supporting information can be downloaded at: https://www. mdpi.com/article/10.3390/app13020922/s1, Supplementary File S1: CARE Checklist of information to include when writing a case report. Supplementary File S2: Timeline. Supplementary File S3: ESAS patient satisfaction evaluation part.

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**Conflicts of Interest:** The authors declare no conflict of interest.

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# CHAPTER 9

General discussion

This chapter is divided into three sections. Section 1 presents the principal findings of this dissertation and how they compare with other studies. Section 2 presents the strengths and limitations of this dissertation and section 3 presents the meaning of the findings of this dissertation (possible explanations and implications for clinicians and policymakers), reported unanswered questions, and future research.

**Section 1. Principal findings of this dissertation and how they compare with other studies**

Chapter 2 presents the protocol for the cross-sectional study on defining, seeking and reporting of adverse effects in systematic reviews of orthodontic interventions. The pilot studies in this protocol confirmed the importance of our research questions. The cross-sectional study (chapter 3) identified 98 eligible systematic reviews of orthodontic interventions. The results showed that a small proportion (36% (35/98)) of these systematic reviews defined seeking adverse effects as an objective. Findings related to adverse effects of interventions were sought in 86% (84/98) of reviews and reviewers reported on these effects in 85% (83/98) of reviews. In 91% (89/98) of the included systematic reviews, the reviewers discussed (weighed) potential adverse effects of interventions anywhere in the review. These outcomes were higher compared to those identified in similar investigations in gastroenterology (67% (52/78)) [1], drug intervention systematic reviews (76% (59/78)) [2], and in Database of Abstracts of Reviews of Effects (DAREs) reviews (48% (38/79)) [2]. The research design, type of intervention, the field of research, and different periods of inclusion of systematic reviews, can explain the differences in the reported proportions between these studies and our results (chapter 3).

A wide variety of different types of adverse effects (n=195) were identified. Based on these findings, we modified the framework of known orthodontic adverse effects reported by Preoteasa et al. [3] and developed a new framework for defining adverse effects of orthodontic interventions (Table 3). Systematic reviews of orthodontic interventions sought and reported predominantly (83% (162/195)) on five types of adverse effects, i.e., (1) tooth structures, (2) periodontal tissues, (3) undesired treatment results, (4) relapse and stability, and (5) negative qualitative experiences by the patient or carer(s).

**Table 3.** Adverse effects hypothetically linked to orthodontic interventions*

| Adverse effects related to | Description |
|---|---|
| Tooth structures | Tooth crown<br>• decalcifications, decays, tooth wear, enamel cracks and fractures; discolorations, deterioration of prosthetic crown (as fracturing a ceramic one during debonding);<br>• iatrogenic damage to the crown, e.g., fracture as a result of trauma tooth root<br>• root resorption, early closure of root apex, ankylosis;<br>• iatrogenic damage to the root, e.g., fracture as a result of trauma tooth pulp<br>• ischemia, pulpitis, necrosis<br>• iatrogenic damage to the pulp, e.g., fracture as a result of trauma |
| Periodontal tissues | • gingivitis, periodontitis, gingival recession or hypertrophy, alveolar bone loss, dehiscences, fenestrations, interdental fold, dark triangles; tooth mobility, plague retention, bacterial count |
| Intraoral (non-tooth or periodontal) tissues | • intraoral tissue irritations and inflammation such as mucosal ulcerations or hyperplasia or irritations of the tongue (as a result of trauma by appliances, e.g., breakage, failure, loosening etc. of appliances or long arch wires)<br>• Scar formation after suturing<br>• chemical burns (e.g., etching related)<br>• thermal injuries (e.g., overheated burs)<br>• nerve damage<br>• tooth eruption, i.e., eruption disturbances (e.g. impactions) caused by orthodontic appliances |
| Extraoral tissues (non-temporomandibular tissues) | • cutting of lips or cheeks, eye injury (e.g., as a result of trauma by appliances, e.g., breakage, failure, loosening etc. of appliances or long arch wires or headgear-related trauma)<br>• discomfort on the lip |
| Temporomandibular tissues and disorders | • temporomandibular tissues and disorders |
| Appliance failure | • breakage, failure, loosening etc. of appliances<br>• long archwires, headgear-related trauma |
| Undesired treatment results | • inadequate morpho-functional, aesthetic or functional final result<br>• inaccuracy of the treatment result<br>• non predictability of the treatment result<br>• Dental side effects e.g. unwanted tipping of teeth, anchorage loss etc.<br>• Skeletal side effects, e.g., unwanted backward rotation of the mandible |
| Relapse and stability | • Relapse and stability of the obtained treatment result |
| Undesired qualitative experiences by the patient or carer(s) | Pain and discomfort<br>• orthodontic tooth movement-related pain and discomfort<br>• appliance (intervention)-related pain and discomfort: i.e., pain and discomfort as a result of the appliance (intervention) itself with or without pain and discomfort associated with tooth movement e.g., tension or pressure of the appliances (constriction of appliances), speech difficulties, eating difficulties, swallowing difficulties, food accumulation, bad tastes and smells<br>• additional intervention-related pain and discomfort, e.g., surgical and non-surgical adjunctive interventions to accelerate tooth movement<br>Tolerability/acceptance/stress issues with the treatment procedures<br>• Absence from work or studies and difficulties in daily activities |

| | |
|---|---|
| | • collaboration (compliance) issues or failure to complete treatment, e.g., dropout<br>• patient anxiety<br>• being teased<br>• social discomfort<br>• embarrassment to wear the appliance<br>• behavioral changes of patients and parents, impaired family relationships<br>• aesthetic look discontents during orthodontic appliance usage<br>• concentration difficulties<br>• reduced enjoyment of food and change in taste<br>• sleeping difficulties<br>• removal of appliance during sleep<br>• development of mannerisms<br><br>Satisfaction with the treatment procedures and final result<br>• not satisfied with the treatment procedures (Check in text what was measured, i.e., during or after)<br>• not satisfied with the final treatment result (Check in text what was measured, i.e., during or after) |
| Gastro-intestinal | • accidental swallowing parts of the orthodontic device (tubes, brackets); |
| Allergy | • Allergies to nickel or latex; |
| Cardio | • infective endocarditis; |
| Chronic fatigue | |
| Cross infections | • from doctor to patient, patient to doctor, patient to patient. |
| Non-defined | Adverse effects that were not defined by the authors of the review: referring to 'any adverse effect', 'any side effect' etc. |
| Additional adverse effects | Additional adverse effects that were identified during data extraction that could not be labeled under any of the categories of adverse effects given in this table |

*Modified from Preoteasa et al. [3]

Chapter 4 presents the protocol for the cross-sectional study described in chapter 5**.** The pilot studies in this protocol confirmed the need to address our research questions on reporting or considering adverse effects in abstracts of systematic reviews of orthodontic interventions and the presence of spin in these abstracts.

The results of this cross-sectional study (chapter 5) showed that 77% (75/98) of the included systematic reviews of orthodontic interventions reported or considered (i.e., discussed, weighted, etc.) potential adverse effects in the abstract. This prevalence was lower i.e., 77% (75/98) than what was reported or considered on adverse effects in the main manuscript of these reviews i.e., 85% (83/98) [4] (chapter 3). The CONSORT (Consolidated Standards of Reporting Trials) harms extension [5], PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) harms extension [6], and the MECIR (Methodological Expectations of Cochrane Intervention Reviews) [7] have all incorporated statements that reporting on adverse effects or findings related to adverse effects is mandatory in abstracts when such findings were sought or reported in the main text. A recent overview of reviews analyzed the changes in reporting adverse effects in abstracts of RCTs over time and found that adverse effects were reported in 47% (258/552) of the abstracts of RCTs before the

publication of the CONSORT harms extension and in 54% (643/1201) of the abstracts of the RCTs published after the publication of this statement [8]. However, caution should be applied when comparing the findings of other studies with our results because of possible differences such as; (1) research designs; (2) sample size; (3) the field of research.

Our research showed that spin on adverse effects in abstracts of systematic reviews of orthodontic interventions was present in 41% (40/98) of the included reviews (chapter 5). Other epidemiolocal research on abstracts of systematic reviews, randomized- and non-randomized studies in different research fields also identified a high prevalence of spin [9, 10, 11, 12, 13, 14, 15, 16]. In the field of orthodontics, spin was found in 49% (53/109) of abstracts of orthodontic meta-analyses [17] and in 62% (69/111) of abstracts of parallel-group RCTs with clearly stated statistically non-significant primary outcomes [18]. Both studies [17, 18] also assessed the association of predictors with the presence of spin. In our study, no associations were found between the presence of spin in the abstracts and any of the predictors (Predictors were: journal, publication year, number of authors, conflict of interest reported, conflict of interest present, funding reported, and type of orthodontic intervention) (Chapter 5). The study by Guo et al. [18] supported our findings regarding the overlapping predictors i.e., 'the year of publication' and 'the number of authors'. In the study by Makou et al. [17] overlap was found for the predictors 'the year of publication' and 'the journal'. However, Makou et al. [17] reported a higher risk of spin in studies with six or more authors. Several variables should be considered when comparing our results with these previous studies [17, 18]. The main variable to consider is that our study only assessed spin on adverse effects in abstracts of systematic reviews. Other variables that could explain differences are: (1) different types and subtypes of spin and the definitions of spin; (2) the location in the text where spin was assessed; (3) the research design; (4) the field of research; (5) the types of interventions; (6) the journals included; and (7) the time point of publication [5].

Our cross-sectional study further showed that misleading reporting (90% (36/40)) on adverse effects was the predominant category of spin in abstracts of systematic reviews of orthodontic interventions. Nascimento et al. [19] reported similar findings, i.e., misleading reporting was the most common type of spin (73% (48/66)) in abstracts of systematic reviews of physiotherapy interventions for low back pain.



Chapter 6 presents the critical appraisal of a systematic review of fixed orthodontic retainers and periodontal health [20]. This systematic review addressed research questions on the possible adverse effects of fixed orthodontic retainers on periodontal health. According to the AMSTAR-2 assessment [21], this review was classified as 'moderate' quality, and overall low risk of bias was assigned using the ROBIS tool [22, 23]. However, ten additional limitations, not covered by the AMSTAR-2 and ROBIS tools, were identified, i.e., two for the methods and eight for the reporting of the systematic review. The critical appraisal pointed out that no recommendations could be made on the best type of fixed retainer to use in clinical practice because (1) the quality of evidence was low for most of the included studies in this review; (2) five out of the 29 included studied reported on poorer periodontal health around fixed retainers; (3) the additional identified limitations in this critical appraisal could have influenced the results of this systematic review.

Chapter 7 presents the critical appraisal of a randomized controlled trial that assessed differences in dental stability, patient perceptions and compliance, and retainer failure after five years of retention, comparing vacuum-formed retainers (VFR) and canine-to canine bonded retainers. According to the Risk of bias 2 tool (RoB2) [24], an overall high risk of bias was assigned, and seven items were not or partially reported according to the CONSORT statement [25]. Additional limitations were identified during the critical appraisal of this RCT. The authors of this RCT [26] reported that most changes were small in both jaws after five years of retention, and only the anterior alignment in the mandible was more stable in the canine-to-canine bonded retainer group. However, this finding is possibly not the result of the retention technique but due to the poor compliance with the VFRs and the inclusion of adolescents only. This critical appraisal showed that the results reported by Krämer et al. [26] should be carefully considered before implementation.

The case report described in chapter 8 presents an adverse effect in orthodontics, which concerns unwanted tooth movements during the retention phase after orthodontic treatment. These movements were probably not the result of dental relapse, but caused by the fixed flexible spiral retainer wire because data at the start of the first orthodontic treatment showed that the original position of the right upper canine differed significantly from the position at the beginning of the second orthodontic treatment phase. This type of unwanted tooth movement combined with a fixed flexible spiral retainer wire has been described previously in orthodontic research in the lower anterior segment [27, 28, 29]. According to Arnold et al., the etiology of these tooth movements consists of forces generated in various ways, i.e., (1) untwisting of the round flexible spiral wires, (2) mechanical deformation of the wire or (3) elastic deflection of the wire [30]. One or more of these generated forces could be the reason for the unwanted tooth movements in this case report. At the completion of the second orthodontic treatment phase, we chose to place fixed braided rectangular retainer wires in the upper and lower jaw since they achieve better torque control [30]. This case report presents a crucial adverse effect in orthodontics. Researchers, patients, and clinicians should be aware of this and recognize this type of unwanted tooth movement early on by organizing regular control visits in the retention phase following orthodontic treatment.

**Section 2. Strengths and limitations of this dissertation**

This dissertation has the following strengths. First, we developed a new framework for defining the adverse effects of orthodontic interventions (Table 3). Second, pilot studies were conducted to calculate the needed sample size, calibrate researchers, and improve our research questions and methodology (chapters 2 and 4). Third, a protocol for each cross-sectional study was developed and published a priori (chapters 2 and 4), which (1) permitted a careful development and planning, including pilot tests, of various research steps, thereby avoiding potential methodological issues; (2) prevented ad hoc decisions during data extraction; (3) reduced the risk of biases, in particular selective (non) reporting bias; and (4) improved transparent reporting and reproducibility [31, 32]. Fourth, all raw data are available in the additional files or were registered in Open Science Framework. Fifth, the protocol presented in chapter 4 was the first publication on spin on adverse effects in systematic reviews of interventions. Sixth, to achieve accurate, complete, and transparent

reporting, we consulted reporting guidelines for both protocols (PRISMA-P 2015 statement [33, 34]) and both cross-sectional studies (STROBE statement [35], PRISMA 2020 statement [36, 37]) and the case report (CARE-guideline [38, 39]) (chapter 2,3,4,5 and 8).

Limitations in this dissertation can be classified as those related to the methods of our cross-sectional studies and those related to the quality of the primary studies included in the eligible systematic reviews of orthodontic interventions. Limitations to the methodology of our cross-sectional studies are: First, the findings reported in the complete orthodontic literature are expected to be worse than those reported in our cross-sectional studies [4, 40] because we only included systematic reviews published in the five leading orthodontic journals and the Cochrane Database of Systematic Reviews. Second, the true magnitude of certain prevalence data (chapters 3 and 5) could be underestimated because we only included recent eligible systematic reviews, i.e., those published between August 1, 2009, and July 21, 2021. However, this period was selected because the inception date coincides with the launch of the PRISMA statement [41, 42]. Third, the assessment of spin is not entirely objective [43]. However, our initial inter-operator agreement for assigning spin was high (Cohen's $\kappa = 0.94$), and complete disagreement was obtained through discussions. Limitations related to the quality of the primary studies included in the eligible systematic reviews of orthodontic interventions are: First, the risk of selective (non) reporting bias because research has shown that adverse effects in both primary research and systematic reviews were poorly assessed and reported [44, 45, 46, 47, 48, 49]. Second, the wide variety of types and definitions of reported adverse effects (chapter 3), made it at times hard to analyze and classify them. This was also reported by Qureshi et al. [50].

**Section 3. The meaning of the findings of this dissertation (possible explanations and implications for clinicians and policymakers), reported unanswered questions and future research.**

This dissertation provides insights into (1) seeking and reporting of adverse effects in systematic reviews of orthodontic interventions, (2) spin on adverse effects in the abstract of systematic reviews of orthodontic interventions, and (3) classifying and defining adverse effects of orthodontic interventions according to our new framework (Table 3). However, more research is needed to investigate the methodology of how reviewers sought and reported adverse effects. This was confirmed in a recent study, which showed that none of the analyzed systematic reviews and meta-analyses followed any guidelines for assessing adverse effects [45]. Research studies should include mandatory information on adverse effects such as definitions of adverse effects, their duration, and time points for assessing them. Research on developing core outcomes for adverse effects [51] and specific guidelines for defining, assessing, and reporting them in both primary studies and systematic reviews are indicated. In addition, systematic reviews that focus exclusively on adverse effects regardless of the condition for which the intervention was performed are necessary [52, 53]. Research is indicated to investigate whether all adverse effects were indeed sought and reported as initially planned in the registered protocols of the included studies. Discrepancies between what was planned for the assessment of adverse effects in protocols registered in PROSPERO and what was reported on these effects in the final review have been reported [54].

The findings in this dissertation could have policy implications for making judgments on accepting or rejecting a systematic review of orthodontic interventions for publication. For example, editors and peer-reviewers should be instructed to adopt various items on adverse effects defined in the Methodological Expectations of Cochrane Intervention Reviews (MECIR) standards [7] and trained to recognize the presence of spin.

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# CHAPTER 10

Summary and conclusions

Chapter 1 introduces the topic of this dissertation. This chapter also presents the objectives, and the definitions used in this dissertation.

Chapters 2, 3, 4, and 5, present the cross-sectional studies on defining, seeking and reporting on adverse effects in systematic reviews of orthodontic interventions. In part 1 of these studies, we assessed defining, seeking and reporting of adverse effects in these reviews. Part 2 focused on the reporting of adverse effects in abstracts of systematic reviews of orthodontic interventions and the presence and type of spin in these abstracts regarding adverse effects. The Cochrane Database of Systematic Reviews and five leading orthodontic journals were searched for eligible reviews published between August 1, 2009, and July 31, 2021. Systematic reviews of orthodontic interventions on human patients of any health status, sex, age, demographics, and socio-economic status and any adverse effect scored at any endpoint or timing were eligible, resulting in the inclusion of 98 systematic reviews.

All study selection and data extraction procedures were conducted by two researchers independently. The results showed that in 84 of 98 (86%) reviews, findings related to adverse effects of orthodontic interventions were sought, and in 83 of 98 (85%) reviews, reviewers reported on them. More than 90% of the reviews considered or discussed potential adverse effects. However, only 36% (35/98) of the reviews defined seeking of adverse effects as a research objective. The Journal of Orthodontics and Craniofacial research had approximately seven times the odds (OR 7.2, 95% CI 1.1 to 48.0) to report that adverse effects were sought in the research objectives compared to the eligible reviews in the Cochrane Database of Systematic Reviews. All identified adverse effects (N=195) were divided into 12 categories according to our new framework for defining adverse effects of orthodontic interventions. Five of these categories accounted for 83% (162/195) of all adverse effects sought and reported. These 5 categories are related to (1) tooth structures, (2) periodontal tissues, (3) undesired treatment results, (4) relapse and stability, and (5) negative qualitative experiences by the patient or carer(s) (Table 8 in chapter 3). Based on the findings of part 1 of our cross-sectional studies, we concluded that most of the included systematic reviews sought and reported adverse effects of orthodontic interventions. However, we have to be cautious when implementing these findings in clinical practice, because of several limitations, i.e., this sample does not represent the complete orthodontic literature, the risk of selective (non) reporting bias regarding adverse effects in the primary studies that were included in the reviews, and unequal assessments of different types of adverse effects, with certain effects being frequently assessed while others rarely or never. (Table 8 in chapter 3).

In part 2 of our cross-sectional studies, we investigated whether adverse effects in systematic reviews of orthodontic interventions were reported or considered in the abstract and whether spin on adverse effects was identified and what type of spin. We also compared the reported adverse effects in the abstract to those sought and reported in the main texts of these reviews. Associations between the presence of spin in the abstracts and variables like the journal, year, number of authors, conflict of interest reported, funding, and type of orthodontic intervention were also assessed. The results showed that 77% (75/98) of the included reviews reported or considered (i.e., discussed, weighed, etc.) potential adverse effects of orthodontic interventions in the abstract. In 41% (40/98) of these reviews, spin regarding adverse effects was present in the abstracts. Misleading reporting was the most

frequent type of spin (90% (36/40). Our univariable logistic regression models (95% CI) showed no associations between the presence of spin in the abstracts of systematic reviews of orthodontic interventions and any of the variables explored. The results of part 2 of our cross-sectional studies showed that findings related to adverse effects reported in the abstract should be interpreted with caution, because abstracts with spin regarding adverse effects, i.e., not being reported or misleading reporting, can make an intervention appear more favorable than it is. End-users should be aware of the presence of spin in abstracts of systematic reviews of orthodontic interventions. Editors and peer-reviewers have an essential role in tackling these problems before systematic reviews of orthodontic interventions are accepted for publication.

Chapter 6 presents the critical appraisal of the systematic review by Arn et al. [1]. The authors assessed the potentially adverse effects of fixed retainers on periodontal health and compared different retainers according to their effects on periodontal health. The results pointed out that fixed orthodontic retainers appear compatible with periodontal health or at least unrelated to severe detrimental effects on the periodontium. However, it has to be considered that 5 out of the 29 included studies showed poorer periodontal health around fixed retainers and the majority of the included evidence was of low quality. In addition, the critical appraisal presented various limitations regarding the methods and reporting of the systematic review.

Chapter 7 presents, the critical appraisal of a randomized controlled trial by Krämer et al. [2]. The authors compared vacuum-formed retainers (VFR) to canine-to-canine bonded retainers in adolescents after five years of retention and assessed differences in dental stability, patient perceptions, compliance and retainer failures. The results showed that for both retention protocols, most post-treatment changes were small in both jaws, but the anterior alignment in the mandible was more stable in the bonded retainer group. This difference is possibly not related to the retention protocol but to the poor compliance identified in the group treated with the VFR and the fact that only adolescents were included. Additional limitations and the high risk of bias in the results of this randomized controlled trial should be considered before implementing its reported findings.

Chapter 8 presents a clinical case that showed unwanted tooth movements during the retention phase following orthodontic treatment. This adverse effect was probably related to the undesired forces of the fixed flexible spiral retainer wire in the upper jaw. After orthodontic retreatment, fixed braided rectangular retainer wires were placed in combination with a vacuum-formed retainer in the upper jaw. The knowledge and awareness of this adverse effect is important for researchers, patients, orthodontists, and dentists. This case report shows the importance of regular control visits after orthodontic treatment.

In chapter 9 the results of this dissertation are discussed. Section 1 presents the principal findings of this dissertation and how they compare with other studies. Section 2 presents the strengths and limitations of this dissertation, and Section 3 presents the meaning of the findings of this dissertation, reported unanswered questions, and future research.

**Conclusions**

Based on the answers to the 12 research questions that were assessed in this dissertation, the following conclusions were made (see 'highlights' page 7):
This dissertation presents a new framework for categorizing and defining adverse effects of orthodontic interventions. Relapse and stability issues and undesired treatment results were the predominant adverse effects sought and reported in systematic reviews of orthodontic interventions, but many adverse effects were underassessed and underreported. This dissertation showed that assessing and reporting of adverse effects of orthodontic interventions in systematic reviews is often not systematic, incomplete, and selective. This dissertation also showed that spin on adverse effects in abstracts of systematic reviews of orthodontic interventions was highly prevalent and that de predominant type of spin was misleading reporting. These findings implicate that what is reported on adverse effects in systematic reviews of orthodontic interventions should be interpreted with caution e.g., when making clinical decisions. Future research should focus on developing, assessing, and reporting of core adverse effects of orthodontic interventions in primary studies and in systematic reviews. Besides conducting traditional systematic reviews of interventions, it is also indicated to conduct systematic reviews that focus exclusively on adverse effects. Multiple stakeholders such as researchers, editors, peer reviewers, and policy makers have to take responsibility and clinicians and patients will ultimately benefit.

## References


1. Arn ML, Dritsas K, Pandis N, Kloukos D. The effects of fixed orthodontic retainers on periodontal health: A systematic review. Am J Orthod Dentofacial Orthop. 2020;157(2):156–164.e17. doi:10.1016/j.ajodo.2019.10.010
2. Krämer A, Sjöström M, Apelthun C, Hallman M, Feldmann I**.** Post-treatment stability after 5 years of retention with vacuum-formed and bonded retainers-a randomized controlled trial. Eur J Orthod 2022; DOI: 10.1093/ejo/cjac043**.**

# CHAPTER 11

Samenvatting en conclusies

Hoofdstuk 1 introduceert het onderwerp van dit proefschrift. In dit hoofdstuk zijn ook de doelstellingen en de in dit proefschrift gebruikte definities opgenomen.

De hoofdstukken 2, 3, 4 en 5 presenteren de *cross-sectional studies* met betrekking tot het definiëren, zoeken en rapporteren van *adverse effects* in *systematic reviews* van orthodontische interventies. In deel 1 van deze studies beoordeelden we het definiëren, zoeken en rapporteren van *adverse effects* in deze *reviews.* Deel 2 richtte zich op het rapporteren van *adverse effects* in samenvattingen van *systematic reviews* van orthodontische interventies en de aanwezigheid en het type *spin* in de samenvatting ten aanzien van deze *adverse effects*. De '*Cochrane Database of Systematic Reviews'* en vijf toonaangevende orthodontische tijdschriften werden doorzocht op in aanmerking komende *reviews* gepubliceerd tussen 1 augustus 2009 en 31 juli 2021. *Systematic reviews* van orthodontische interventies bij patiënten van elke gezondheidsstatus, geslacht, leeftijd, demografie en sociaaleconomische status en elk nadelig effect waargenomen op elk eindpunt of tijdstip kwamen in aanmerking, hetgeen resulteerde in de inclusie van 98 *systematic reviews*.

Alle studie selectie en data-extractie procedures zijn door twee onderzoekers onafhankelijk van elkaar uitgevoerd. De resultaten lieten zien dat in 84 van de 98 (86%) *reviews* werd gezocht naar bevindingen met betrekking tot *adverse effects* van orthodontische interventies en dat in 83 van de 98 (85%) *reviews* de *reviewers* daarover rapporteerden. Meer dan 90% van de *reviews* beschouwde of bediscussieerde potentiële *adverse effects* in de *reviews.* Echter, slechts 36% (35/98) van de *reviews* definieerde het zoeken van *adverse effects* als een onderzoeksdoelstelling. In het tijdschrift '*The Journal of Orthodontics and Craniofacial research'* was de kans ongeveer zeven keer zo groot (OR 7.2, 95% CI 1.1 to 48.0) dat de gezochte *adverse effects* werden gerapporteerd in de onderzoeksdoelstellingen in vergelijking tot de in aanmerking komende *reviews* in de '*Cochrane Database of Systematic Reviews'*. Alle geïdentificeerde *adverse effects* (N=195) werden ingedeeld in 12 categorieën volgens ons nieuwe *framework* voor het definiëren van *adverse effects* van orthodontische interventies. Drieëntachtig procent (162/195) van alle gezochte en gerapporteerde *adverse effects* vielen onder vijf van deze categorieën. Deze 5 categorieën hebben betrekking op (1) tandstructuren, (2) parodontale weefsels, (3) ongewenste behandelresultaten, (4) terugval en stabiliteit en (5) negatieve kwalitatieve ervaringen van de patiënt of verzorger(s) (tabel 8 in hoofdstuk 3). Op basis van de resultaten van deel 1 van onze *cross-sectional studies*, concludeerden wij dat de meeste van de geïncludeerde *systematic reviews, adverse effects* van orthodontische interventies zochten en rapporteerden. We moeten echter voorzichtig zijn met het interpreteren van deze data vanwege verschillende beperkingen: 1) deze studies vertegenwoordigen niet de volledige orthodontische literatuur, 2) het risico op *selective (non) reporting bias* in de primaire studies die in de *reviews* zijn opgenomen en 3) ongelijke beoordeling van verschillende *adverse effects*, waarbij bepaalde *adverse effects* vaak werden beoordeeld en andere zelden of nooit (tabel 8 in hoofdstuk 3).

In deel 2 van onze *cross-sectional studies* onderzochten wij of in *systematic reviews* van orthodontische interventies *adverse effects* werden gerapporteerd of beschouwd in de samenvatting en of er sprake was van *spin* met betrekking tot de onderzochte *adverse effects* en welk type *spin*. De in de samenvatting gerapporteerde *adverse effects* hebben we ook vergeleken met de gezochte en gerapporteerde *adverse effects* in de hoofdteksten van

deze *reviews*. Verbanden tussen de aanwezigheid van *spin* in de samenvattingen en variabelen zoals het tijdschrift, jaartal, aantal auteurs, gerapporteerde belangenverstrengeling, financiering en type orthodontische interventie zijn ook beoordeeld. Uit de resultaten bleek dat 77% (75/98) van de geïncludeerde *reviews* in de samenvatting mogelijke *adverse effects* van orthodontische interventies rapporteerden of beschouwden (d.w.z. bediscussieerde, afwoog, enz.). In 41% (40/98) van deze *reviews* was er sprake van *spin* met betrekking tot *adverse effects* in de samenvatting. *Misleading reporting* was het meest voorkomende type *spin* (90% (36/40)). Onze univariabele logistische regressiemodellen (95% CI) lieten geen verbanden zien tussen de aanwezigheid van *spin* in de samenvattingen van *systematic reviews* van orthodontische interventies en de onderzochte variabelen. De resultaten van deel 2 van onze *cross-sectional studies* toonden aan dat resultaten met betrekking tot *adverse effects* gerapporteerd in de samenvatting voorzichtig moeten worden geïnterpreteerd, omdat samenvattingen met *spin* ten aanzien van *adverse effects*, d.w.z. niet gerapporteerd of misleidend gerapporteerd, een interventie gunstiger kunnen doen lijken dan deze is. Eindgebruikers moeten zich bewust zijn van de aanwezigheid van *spin* in samenvattingen van *systematic reviews* van orthodontische interventies. Redacteuren en *peer-reviewers* spelen een essentiële rol bij het aanpakken van deze problemen alvorens *systematic reviews* van orthodontische interventies worden geaccepteerd voor publicatie.

Hoofdstuk 6 presenteert de kritische beoordeling van het *systematic review* van Arn et al. [1]. De auteurs vergeleken de mogelijke *adverse effects* van verschillende vaste retentiedraden op de parodontale gezondheid. De resultaten wezen erop dat vaste retentiedraden compatibel lijken met de parodontale gezondheid of in ieder geval geen verband houden met ernstige schadelijke effecten op het parodontium. Er moet echter rekening worden gehouden met het gegeven dat 5 van de 29 geïncludeerde studies een slechtere parodontale gezondheid lieten zien rondom vaste retentiedraden en dat het merendeel van het geïncludeerde *evidence* van lage kwaliteit was. Daarnaast liet de kritische beoordeling verschillende beperkingen zien met betrekking tot de methoden en de rapportage van het *systematic review*.

Hoofdstuk 7 presenteert de kritische beoordeling van een *RCT* van Krämer et al. [2]. De auteurs vergeleken vacuümgevormde retentie apparatuur met vaste retentiedraden van hoektand tot hoektand bij adolescenten na vijf jaar retentie en beoordeelden verschillen in gebitsstabiliteit, patiëntpercepties, therapietrouw en het falen van de retentie apparatuur. De resultaten lieten zien dat voor beide retentie protocollen de meeste veranderingen na de behandeling klein waren in beide kaken, maar dat het orthodontisch behandelde (opgelijnde) onderfront stabieler was in de groep met vaste retentiedraden. Dit verschil houdt mogelijk geen verband met het retentie protocol, maar met de slechte naleving van de therapie geïdentificeerd in de groep die behandeld werd met de vacuümgevormde retentie apparatuur en het feit dat alleen adolescenten werden geïncludeerd. Aanvullende beperkingen en het hoge risico op bias in de resultaten van deze *RCT* moeten in acht genomen worden alvorens de gerapporteerde resultaten worden geïmplementeerd.

Hoofdstuk 8 presenteert een klinische casus die ongewenste tandbewegingen liet zien tijdens de retentiefase na een orthodontische behandeling. Dit *adverse effect* hield waarschijnlijk verband met de ongewenste krachten van de vaste flexibele spiraalvormige

retentiedraad in de bovenkaak. Na orthodontische herbehandeling werden vaste gevlochten rechthoekige retentiedraden geplaatst in combinatie met vacuümgevormde retentie apparatuur in de bovenkaak. De kennis en het bewustzijn van dit *adverse effect* is belangrijk voor onderzoekers, patiënten, orthodontisten en tandartsen. Dit *case report* laat het belang zien van regelmatige controlebezoeken na een orthodontische behandeling.

In hoofdstuk 9 worden de resultaten van dit proefschrift besproken. Deel 1 presenteert de belangrijkste bevindingen van dit proefschrift en hoe deze zich verhouden tot andere studies. Deel 2 presenteert de sterke punten en beperkingen van dit proefschrift en deel 3 presenteert de betekenis van de bevindingen van dit proefschrift, gerapporteerde onbeantwoorde vragen en toekomstig onderzoek.

**Conclusies**

De volgende conclusies werden getrokken op basis van de antwoorden op de 12 onderzoeksvragen in dit proefschrift (zie '*highlights*' pagina 7):
Dit proefschrift presenteert een nieuw *framework* voor het categoriseren en definiëren van *adverse effects* van orthodontische interventies. *Relapse*, problemen met stabiliteit en ongewenste behandelresultaten waren de belangrijkste *adverse effects* die werden gezocht en gerapporteerd in *systematic reviews* van orthodontische interventies, maar veel *adverse effects* werden onvoldoende beoordeeld en onvoldoende gerapporteerd. Dit proefschrift toonde aan dat het beoordelen en rapporteren van *adverse effects* van orthodontische interventies in *systematic reviews* vaak onvolledig was, niet systematisch en selectief. Dit proefschrift toonde ook aan dat *spin* met betrekking tot *adverse effects* in samenvattingen van *systematic reviews* van orthodontische interventies veel voorkwam en dat het meest prevalente type *spin misleading reporting* was. Deze bevindingen impliceren dat wat gerapporteerd wordt over *adverse effects* in *systematic reviews* van orthodontische interventies voorzichtig geïnterpreteerd moet worden, bijvoorbeeld met het maken klinische beslissingen. Toekomstig onderzoek zou zich moeten richten op het ontwikkelen, beoordelen en rapporteren van '*core-adverse effects'* van orthodontische interventies in primaire studies en in *systematic reviews.* Naast het uitvoeren van traditionele *systematic reviews* van interventies, is het ook geïndiceerd om *systematic reviews* die zich uitsluitend richten op *adverse effects* uit te voeren. Meerdere belanghebbenden zoals onderzoekers, redacteuren, *peer reviewers* en beleidsbepalers moeten hun verantwoordelijkheid nemen en uiteindelijk zullen clinici en patiënten hiervan profiteren.

## Referenties


1. Arn ML, Dritsas K, Pandis N, Kloukos D. The effects of fixed orthodontic retainers on periodontal health: A systematic review. Am J Orthod Dentofacial Orthop. 2020;157(2):156–164.e17. doi:10.1016/j.ajodo.2019.10.010
2. Krämer A, Sjöström M, Apelthun C, Hallman M, Feldmann I**.** Post-treatment stability after 5 years of retention with vacuum-formed and bonded retainers-a randomized controlled trial. Eur J Orthod 2022; DOI: 10.1093/ejo/cjac043**.**

# CHAPTER 12

## List of publications

Peer-reviewed full-text publications

*In this dissertation*

Steegmans PAJ, Bipat S, Meursinge Reynders RA. Seeking adverse effects in systematic reviews of orthodontic interventions: protocol for a cross-sectional study. Syst Rev. 2019 Apr 5;8(1):89.

Steegmans PAJ, Di Girolamo N, Meursinge Reynders RA. Spin in the reporting, interpretation, and extrapolation of adverse effects of orthodontic interventions: protocol for a cross-sectional study of systematic reviews. Res Integr Peer Rev. 2019 Dec 19;4:27.

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Steegmans PAJ, Di Girolamo N, Meursinge Reynders RA. Spin on adverse effects in abstracts of systematic reviews of orthodontic interventions: a cross-sectional study (part 2). Syst Rev. 2023 Jun 20;12(1):99.

Steegmans PAJ, Meursinge Reynders RA. Fixed orthodontic retainers and periodontal health. Evid Based Dent. 2020 Dec;21(4):146-149.

Steegmans PAJ, Cavagnetto D, Meursinge Reynders RA. Which orthodontic retention protocol should I implement? A critical assessment of a randomized controlled trial. Evid Based Dent. 2022 Dec;23(4):162-165.

Steegmans PAJ, Jonkman REG, de Lange J. Fixed Flexible Spiral Wire Retainers and Unwanted Tooth movements: A Case Report. *Appl. Sci.* 2023, *13*(2), 922.

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## Author's contributions

**Chapter 2**

*Published as:*
Seeking adverse effects in systematic reviews of orthodontic interventions: protocol for a cross-sectional study.

*Authors:*
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*Published in:* Systematic Reviews, 2019

*Author contributions:*
Conceived and designed: RMR, PS
Performed the study: RMR, PS
Analyzed the data: RMR, SB, PS
Critically revised the manuscript: RMR, SB, PS

**Chapter 3**

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*Authors:* Steegmans PAJ, Di Girolamo N, Bipat S, Meursinge Reynders RA

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*Author contributions:*
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Performed the study: RMR, PS
Analyzed the data: RMR, NDG, SB, PS
Critically revised the manuscript: RMR, NDG, SB, PS

**Chapter 4**

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Spin in the reporting, interpretation, and extrapolation of adverse effects of orthodontic interventions: protocol for a cross-sectional study of systematic reviews.

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Steegmans PAJ, Di Girolamo N, Meursinge Reynders RA

*Published in:* Research Integrity and Peer Review, 2019

*Author contributions:*
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Analyzed the data: RMR, NDG, PS
Critically revised the manuscript: RMR, NDG, PS

**Chapter 5**

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*Published in:* Systematic reviews, 2023

*Author contributions:*
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Analyzed the data: RMR, NDG, PS
Critically revised the manuscript: RMR, NDG, PS

**Chapter 6**

*Published as:* Fixed orthodontic retainers and periodontal health.

*Authors:*
Steegmans PAJ, Meursinge Reynders RA.

*Published in:* Evidence Based Dentistry, 2020

*Author contributions:*
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Performed the study: RMR, PS
Analyzed the data: RMR, PS
Critically revised the manuscript: RMR, PS

**Chapter 7**

*Published as:* Which orthodontic retention protocol should I implement? A critical assessment of a randomized controlled trial

*Authors:* Steegmans PAJ, Cavagnetto D, Meursinge Reynders RA.

*Published in:* Evidence-Based Dentistry , 2022

*Author contributions:*
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Performed the study: DC, RMR, PS
Analyzed the data: DC, RMR, PS
Critically revised the manuscript: DC, RMR, PS

**Chapter 8**

*Published as:* Fixed flexible spiral wire retainers and unwanted tooth movements: a Case Report

*Authors:* JL, RJ, PS

*Published in:* Applied Sciences

*Author contributions:*
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Performed the study: PS
Analyzed the data: JL, RJ, PS
Critically revised the manuscript: JL, RJ, PS

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## Conflict of interest

RMR and SB are both Associate Editors for Systematic Reviews. All authors declare that they have no further competing interests.

## Data sharing statement

All data are presented in the additional files and raw data have been placed in the Open Science Framework (https://osf.io/ka7mp/)

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Springer Nature
[online] Available from:
https://www.nature.com/nature-portfolio/reprints-and-permissions (accessed July 5th 2023

MDPI
[online] Available from:
https://www.mdpi.com/authors/rights (accessed July 5th 2023)

# CHAPTER 13

# Additional files chapter 2

**Additonal file 1. PRISMA-P Checklist**

## PRISMA-P 2015 Checklist

This checklist has been adapted for use with systematic review protocol submissions to BioMed Central journals from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1

An Editorial from the Editors-in-Chief of *Systematic Reviews* details why this checklist was adapted - Moher D, Stewart L & Shekelle P: Implementing PRISMA-P: recommendations for prospective authors. *Systematic Reviews* 2016 5:15

| Section/topic | # | Checklist item | Information reported | | Line number(s) |
|---|---|---|---|---|---|
| | | | Yes | No | |
| **ADMINISTRATIVE INFORMATION** | | | | | |
| **Title: Seeking adverse effects in systematic reviews of orthodontic interventions: protocol for a cross-sectional study** | | | | | |
| Identification | 1a | Identify the report as a protocol of a systematic review | x | ☐ | line 2 |
| Update | 1b | If the protocol is for an update of a previous systematic review, identify as such | ☐ | x | Not applicable |
| **Registration** | 2 | If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract | ☐ | x | Not applicable |
| **Authors** | | | | | |
| Contact | 3a | Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author | x | ☐ | lines 24-28 |
| Contributions | 3b | Describe contributions of protocol authors and identify the guarantor of the review | x | ☐ | Lines 360-365 |
| **Amendments** | 4 | If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments | ☐ | x | Not applicable |
| **Support** | | | | | |
| Sources | 5a | Indicate sources of financial or other support for the review | x | ☐ | Lines 356-358 |
| Sponsor | 5b | Provide name for the review funder and/or sponsor | ☐ | x | Not applicable |
| Role of sponsor/funder | 5c | Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol | ☐ | x | Not applicable |
| **INTRODUCTION** | | | | | |
| **Rationale** | 6 | Describe the rationale for the review in the context of what is already known | x | ☐ | Lines 89-128 |

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| Section/topic | # | Checklist item | Information reported | | Line number(s) |
|---|---|---|---|---|---|
| | | | Yes | No | |
| **Objectives** | 7 | Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) | x | ☐ | Lines 132-142 |
| **METHODS** | | | | | |
| **Eligibility criteria** | 8 | Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review | x | ☐ | Lines 156-201 |
| **Information sources** | 9 | Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage | x | ☐ | Lines 204-213 |
| **Search strategy** | 10 | Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated | x | ☐ | Lines 204-213 |
| ***STUDY RECORDS*** | | | | | |
| Data management | 11a | Describe the mechanism(s) that will be used to manage records and data throughout the review | x | ☐ | Lines 217-226 |
| Selection process | 11b | State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis) | x | ☐ | Lines 227-237 |
| Data collection process | 11c | Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators | x | ☐ | Lines 238-252 |
| **Data items** | 12 | List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications | x | ☐ | Lines 238-263 |
| **Outcomes and prioritization** | 13 | List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale | x | ☐ | Lines 265-277 |
| **Risk of bias in individual studies** | 14 | Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis | ☐ | x | Not applicable |
| ***DATA*** | | | | | |
| **Synthesis** | 15a | Describe criteria under which study data will be quantitatively synthesized | ☐ | x | Not applicable |
| | 15b | If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., $I^2$, Kendall's tau) | ☐ | x | Not applicable |

| Section/topic | # | Checklist item | Information reported | | Line number(s) |
|---|---|---|---|---|---|
| | | | Yes | No | |
| | 15c | Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression) | ☐ | x | Not applicable |
| | 15d | If quantitative synthesis is not appropriate, describe the type of summary planned | ☐ | x | Not applicable |
| **Meta-bias(es)** | 16 | Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies) | ☐ | x | Not applicable |
| **Confidence in cumulative evidence** | 17 | Describe how the strength of the body of evidence will be assessed (e.g., GRADE) | ☐ | x | Not applicable |

**Additional file 2. Pilot tests**

Eligible systematic reviews of orthodontic interventions published in the eligible journals were used for our pilot tests and were stratified evenly over the eligible years and journals. We calculated the required sample size of our pilot study based on the probability of Yes scores for our primary research question 'Did the review seek any findings related to adverse effects of interventions in the included studies?

To calculate this sample size we used the following equation [24]:

$$n = \frac{\ln(1-\Upsilon)}{\ln(1-\pi)}$$

n = the sample size for the pilot study

$\Upsilon$ = the threshold of confidence (95%)

$\pi$ = the probability of a 'Yes' score

We calculated the sample size separately for systematic reviews of orthodontic interventions in the Cochrane Database of Systematic Reviews and those published in the 5 leading orthodontic journals. We used the probabilities of the Yes scores identified during our scoping searches as our benchmark. These probabilities were respectively 1 and 0.25. Based on these probabilities we calculated the required sample sizes of respectively 1 and 10.4. To play it safe we planned to include at least 2 Cochrane reviews and 12 orthodontic reviews in our pilot study. We planned increasing the size of the pilot study when the probability of yes scores for the pertinent review types would be inferior in the pilot studies compared to those identified in the scoping searches. We used random number generator software [25] to select the pilot reviews. We searched the first eligible review published in the random issue number of the pertinent journal for the years 2009, 2010, and 2011. If no eligible review was identified for that issue, we searched the first eligible review published in subsequent issues of the stratified journal subgroup. If no eligible reviews were identified for that period, we searched in the issues published prior to the random issue number and back to the starting issue of the stratified journal subgroup. We applied this strategy for the 3 stratified subgroups, i.e., 2009-2011, 2012-2014, 2015-2017 (Table). The prevalence of eligible systematic reviews that sought any findings related to adverse effects in the included studies was 25% (3/12) for the orthodontic journals and 100% (2/2) for reviews identified in the Cochrane Database of Systematic reviews.

**Table. Systematic reviews of orthodontic interventions selected for the pilot test**

| Journal | Year and number of issues | Random issue number | Selected systematic review |
|---|---|---|---|
| Cochrane Database of Systematic reviews | 2009, 2010, and 2011 (28 issues) | 24 | No reference identified |
| Cochrane Database of Systematic reviews | 2012, 2013, and 2014 (36 issues) | 31 | Agostino P, Ugolini A, Signori A, Silvestrini-Biavati A, Harrison JE, Riley P. Orthodontic treatment for posterior crossbites. Cochrane Database Syst Rev. 2014 Aug 8;(8):CD000979. |
| Cochrane Database of Systematic reviews | 2015, 2016, and 2017 (36 issues) | 12 | Littlewood SJ, Millett DT, Doubleday B, Bearn DR, Worthington HV. Retention procedures for stabilising tooth position after treatment with orthodontic braces Cochrane Database Syst Rev. 2016 Jan 29;(1):CD002283. |
| European Journal of Orthodontics | 2009, 2010, and 2011 (18 issues) | 10 | Naoumova J, Kurol J, Kjellberg H. A systematic review of the interceptive treatment of palatally displaced maxillary canines. Eur J Orthod. 2011 Apr;33(2):143-9. |
| European Journal of Orthodontics | 2012, 2013, and 2014 (18 issues) | 5 | Zuccati G, Casci S, Doldo T, Clauser C. Expansion of maxillary arches with crossbite: a systematic review of RCTs in the last 12 years. Eur J Orthod. 2013 Feb;35(1):29-37. |
| European Journal of Orthodontics | 2015, 2016, and 2017 (18 issues) | 3 | Koretsi V, Zymperdikas VF, Papageorgiou SN, Papadopoulos MA. Treatment effects of removable functional appliances in patients with Class II malocclusion: a systematic review and meta-analysis. Eur J Orthod. 2015 Aug;37(4):418-34. |
| American Journal of Orthodontics and Dentofacial Orthopedics | 2009, 2010, and 2011 (36 issues) | 18 | Chen SS, Greenlee GM, Kim JE, Smith CL, Huang GJ. Systematic review of self-ligating brackets. Am J Orthod Dentofacial Orthop. 2010 Jun;137(6):726.e1-726.e18; discussion 726-7. |
| American Journal of Orthodontics and Dentofacial Orthopedics | 2012, 2013, and 2014 (36 issues) | 35 | Yang X, Li C, Bai D, Su N, Chen T, Xu Y, Han X. Treatment effectiveness of Fränkel function regulator on the Class III malocclusion: a systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2014 Aug;146(2):143-54. |
| American Journal of Orthodontics and Dentofacial Orthopedics | 2015, 2016, and 2017 (36 issues) | 9 | Nucera R, Lo Giudice A, Rustico L, Matarese G, Papadopoulos MA, Cordasco G. Effectiveness of orthodontic treatment with functional appliances on maxillary growth in the short term: A systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2016 May;149(5):600-611.e3. |
| Angle Orthodontist | 2009, 2010, and 2011 (18 issues) | 6 | Leonardi R, Annunziata A, Licciardello V, Barbato E. Soft tissue changes following the extraction of premolars in nongr owing patients with bimaxillary protrusion. A systematic review. Angle Orthod. 2010 Jan;80(1):211-6. |
| Angle Orthodontist | 2012, 2013, and 2014 (18 issues) | 4 | Feng X, Li J, Li Y, Zhao Z, Zhao S, Wang J. Effectiveness of TAD-anchored maxillary protraction in latemixed dentition. Angle Orthod. 2012 Nov;82(6):1107-14. |
| Angle Orthodontist | 2015, 2016, and 2017 (18 issues) | 13 | Diar-Bakirly S, Feres MF, Saltaji H, Flores-Mir C, El-Bialy T. Effectiveness of the transpalatal arch in controlling orthodontic anchorage in maxillary premolar extraction cases: A systematic review and meta-analysis.Angle Orthod. 2017 Jan;87(1):147-158. |
| The Korean Journal of Orthodontics | 2009, 2010, and 2011 (18 issues) | 7 | No reviews identified in all 18 issues |
| The Korean Journal of Orthodontics | 2012, 2013, and 2014 | 14 | No reviews identified in all 18 issues |

| | | | |
|---|---|---|---|
| | (18 issues) | | |
| The Korean Journal of Orthodontics | 2015, 2016, and 2017 (18 issues) | 7 | Papageorgiou SN, Höchli D, Eliades T. Outcomes of comprehensive fixed appliance orthodontic treatment: A systematic review with meta-analysis and methodological overview. Korean J Orthod. 2017 Nov; 47(6): 401–413. |
| Orthodontics and Craniofacial Research | 2009, 2010, and 2011 (12 issues) | 1 | Several reviews were identified, but none were eligible |
| Orthodontics and Craniofacial Research | 2012, 2013, and 2014 (12 issues) | 3 | Cordasco G, Matarese G, Rustico L, Fastuca S, Caprioglio A, Lindauer SJ, Nucera R. Efficacy of orthopedic treatment with protraction facemask on skeletal Class III malocclusion: a systematic review and meta-analysis. Orthod Craniofac Res. 2014 Aug;17(3):133-43. |
| Orthodontics and Craniofacial Research | 2015, 2016, and 2017 (12 issues) | 1 | Al-Saleh MA, Alsufyani N, Flores-Mir C, Nebbe B, Major PW. Changes in temporomandibular joint morphology in class II patien ts treated with fixed mandibular repositioning and evaluated thro ugh 3D imaging: a systematic review. Orthod Craniofac Res. 2015 Nov;18(4):185-201. |

## Additional file 3. Search terms and their derivatives

**Table. Search terms and their derivatives**

| Search terms and their derivatives | Search terms for searching multiple words in a PDF |
|---|---|
| “adverse” | ADVERSE, Adverse, adverse |
| “effect”, “effects” | EFFECT, Effect, effect |
| “reaction”, “reactions” | REACTION, Reaction, reaction |
| “complication”, “complications”, “complicated”, “complicating” | COMPLICAT, Complicat, complicat |
| “harm”, “harms”, “harmful” | HARM, Harm, harm |
| “risk”, “risks”, “risky” | RISK, Risk, risk |
| “safe”, “safety” | SAFE, Safe, safe |
| “side” | SIDE, Side, side |
| “toxic”, “toxicity” | TOXIC, Toxic, toxic |
| “benefit”, “benefits” | BENEFIT, Benefit, benefit |
| “result”, “results” | RESULT, Result, result |
| “finding”, “findings” | FINDING, Finding, finding |
| “outcome”, “outcomes” | OUTCOME, Outcome, outcome |
| “limitation”, “limitations”, limit | LIMIT, Limit, limit |
| “damage”, “damages”, “damaging” | DAMAGE, Damage, damage |
| “data” | DATA, Data, data |
| “information” | INFO, Info, info |
| “conflict”, “conflicts”, “conflicting” | CONFLICT, Conflict, conflict |
| “negative” | NEGATIVE, Negative, negative |
| “detrimental” | DETRIMENTAL, Detrimental, detrimental |
| “disadvantage”, “disadvantages”, “disadvantageous” | DISADVAN, Disadvan, disadvan |
| “down” | DOWN, Down, down |
| “injury”, “injuries”, “injured”, “injurious” | INJUR, Injur, injur |
| “byproduct”, “byproducts” | BYPRODUCT, Byproduct, byproduct |
| “collateral” | COLLATERAL, Collateral, collateral |
| “unfavorable”, “unfavourable” | UNFAVO, Unfavo, unfavo |
| “destructive” | DESTRUCT, Destruct, destruct |
| “unsafe” | UNSAFE, Unsafe, unsafe |
| “undesired”, “undesirable” | UNDESIR, Undesir, undesir |
| “recommend”, “recommendation”, “recommending” | RECOMMEND, Recommend, recommend |
| “emergency”, “emergencies” | EMERGEN, Emergen, emergen |

## Additional file 4. Data collection forms

**Table. Data collection forms***

| Items for the main manuscript | Description |
|---|---|
| Journal | List the pertinent journal |
| Year | Year of publication |
| Binder page number | List the binder page number |
| Reference | List full reference (Authors, Title, Journal) |
| Is the article a systematic review? | Answer: Yes/No<br>Consider definition of a systematic review |
| What type of systematic review? | List the type of systematic review.<br>Consider different types of systematic reviews.<br>When the publication is not an intervention systematic review describe what type it is or could be and classify. Types of systematic reviews will receive a final classification during the discussions between operators. |
| Were orthodontic interventions assessed? | Answer: Yes/No<br>Consider the definition of orthodontic interventions. |
| What was the orthodontic intervention? | List the type of orthodontic intervention<br>NA: When the article is not a systematic review or not a systematic review of interventions. |
| Is the systematic review eligible? | Answer: Yes/No<br>Yes: The article is a systematic review of an orthodontic intervention.<br>No: The article is not a systematic review of an orthodontic intervention.<br>No: The article is a systematic review of an orthodontic intervention, but focusses exclusively on its adverse effects. |
| Page and potential comments** | Present the pertinent pages of reference for scoring the previous items and list the potential comments. |
| Was seeking of adverse effects of interventions defined as a research objective of the review? | Answer: Yes/No<br>Yes: When seeking of adverse effects of interventions was defined as a research objective or as a research question or when adverse effects were predefined a priori as outcomes to assess.<br>No: Seeking of adverse effects of interventions was not defined as a research objective or as a research question or when adverse effects were not predefined a priori as outcomes to assess. |
| What adverse effects of interventions were defined as research objectives? | Answer: List adverse effects/NA<br>List all adverse effects of interventions that the reviewers defined as research objectives.<br>NA: When the following question was answered with a 'No': 'Was seeking of adverse effects of interventions defined as a research objective of the review?' |
| Did the review seek any findings related to adverse effects of interventions in the included studies? | Answer: Yes/No<br>Yes: Any findings related to adverse effects of interventions in the included studies were sought by the reviewers.<br>Seeking any findings related to adverse effects of interventions in the included studies refers to reporting anywhere in the review (except in the |

| | |
|---|---|
| | Abstract) that such adverse effects in the included studies were sought.<br>Yes: Yes is also scored when reviewers only reported findings related to adverse effects of interventions in the included studies, but did not report that they actually sought them or planned to seek them. For example 'Yes' will be scored when outcomes on adverse effects of interventions in the included studies were reported in the review, but were not defined as objectives of the review.<br>Yes: Yes is also scored when the reviewers reported that they planned to seek (for example in the research objectives) findings related to adverse effects of interventions in the included studies, but did not report on these findings.<br>No: Findings related to adverse effects of interventions in the included studies were not sought by the reviewers. |
| Did the review report findings related to adverse effects of interventions sought in the included studies? | Answer: Yes/No/NA<br>Yes: The review reported findings related to adverse effects of interventions sought in the included studies.<br>'Yes' is also scored when the review reported that no findings on adverse effects of interventions in the included studies were identified.<br>No: The review did not report any findings related to adverse effects of interventions sought in the included studies.<br>NA: When the following question was answered with a No: 'Did the review seek any findings related to adverse effects of interventions in the included studies?' |
| What findings related to adverse effects of interventions sought in the included studies were reported in the review? | Answer: List of adverse effects/NA<br>List all findings related to adverse effect(s) of interventions that were identified in the included studies and reported in the review.<br>NA: When the following question was answered with a 'No': 'Did the review seek any findings related to adverse effects of interventions in the included studies?' |
| Rationale for assigning an effect as 'adverse' or 'not adverse' (In case of additional or ambivalent adverse effects) | Answer: Present the rationale for assigning an effect as 'adverse' or 'not adverse' (In case of additional or ambivalent adverse effects) |
| Page and potential comments** | Present the pertinent pages of reference for scoring the previous items and list the potential comments. |
| Were potential adverse effects of the intervention considered, discussed (weighed) anywhere in the review? | Answer: Yes/No<br>Yes: Potential adverse effect(s) of interventions in the included studies were sought and reported by the reviewers. 'Yes' is also scored when potential adverse effect(s) of interventions were not sought, but only considered, discussed (weighed) anywhere in the review.<br>'No' is scored when potential adverse effects of the intervention were not considered, discussed (weighed) anywhere in the review. |

| | |
|---|---|
| Rationale for assigning an effect as 'adverse' or 'not adverse' (In case of additional or ambivalent adverse effects) | Answer: Present the rationale |
| Page and potential comments** | Present the pertinent pages of reference for scoring the previous items and list the potential comments. |

*To address our research question we will not consider what was reported regarding this question in the abstract and in the protocol of the review.

**When referring to a particular page in the systematic review, we will use the page number of the systematic review and not the number in the binder document.

## Additional files chapter 3

**Additional file 1. STROBE checklist**

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

| | Item No | Recommendation | Page No |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 2 and 3 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 3 and 4 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 5 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 5 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6 and 7 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants | 6 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 8 and 9 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 8 and 9 |
| Bias | 9 | Describe any efforts to address potential sources of bias | NA |
| Study size | 10 | Explain how the study size was arrived at | 8 and 9 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 9 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 9 |

| | | | |
|---|---|---|---|
| | | (*b*) Describe any methods used to examine subgroups and interactions | 9 |
| | | (*c*) Explain how missing data were addressed | 9 |
| | | (*d*) If applicable, describe analytical methods taking account of sampling strategy | NA |
| | | (*e*) Describe any sensitivity analyses | NA |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 9 and 10 |
| | | (b) Give reasons for non-participation at each stage | NA |
| | | (c) Consider use of a flow diagram | 10 |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 10 |
| | | (b) Indicate number of participants with missing data for each variable of interest | NA |
| Outcome data | 15* | Report numbers of outcome events or summary measures | 10 and 11 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 10 and 11 |
| | | (*b*) Report category boundaries when continuous variables were categorized | NA |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | NA |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 11 |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 11 and 12 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 12 and 13 |

| | | | |
|---|---|---|---|
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 13 and 14 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 14 |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 15 |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

## Additional file 2

**Table of contents for additional file 2**

| Additional file item | Description |
|---|---|
| Additional file 2A | Difference between the protocol and the completed cross-sectional study |
| Additional file 2B | Selected journals and their 2018 impact factor (Clarivate Analytics 2021) |
| Additional file 2C | Data collection forms |
| Additional file 2D | Adverse effects hypothetically linked to orthodontic interventions according to Preoteasa et al. (2012) |
| Additional file 2E | Adverse effects hypothetically linked to orthodontic interventions |
| References for additional file 2 | References for additional file 2 |

**Additional file 2A. Differences between the protocol and the completed cross-sectional study**

| Differences between the protocol and the completed cross-sectional study | Rationale |
|---|---|
| Extension of the search period to identify eligible systematic reviews | We planned to complete our study on July 31 2019, but as a result of COVID 19-related delays we extended our search period to July 31 2021. |
| Excluding systematic reviews with Bayesian network meta-analysis | We excluded systematic reviews with Bayesian network meta-analyses, because such reviews include the results of multiple interventions, which could make it difficult to understand which adverse effect was assigned to which specific intervention. |
| Excluding systematic reviews that did not assess a specific orthodontic intervention, but refer to orthodontic interventions as a whole. | We excluded systematic reviews that did not assess a specific orthodontic intervention, but referred to orthodontic interventions as a whole. |
| Excluding systematic reviews that were conducted by one operator only | We excluded reviews that were conducted by one reviewer only, because such an approach is often conducted for narrative reviews, but is not congruent with the systematic approach of systematic reviews. |
| Implementing univariable logistic regression models in the statistical analyses | We implemented univariable logistic regression models to determine the association between each of the 4 outcomes and the journal in which the SR was published using the Cochrane Database of Systematic Reviews as reference. Chi-square tests of independence as planned in our protocol were not used, because of the small number of systematic reviews in each eligible journal and the low variability in the response scored (prevalence of 'no' ranging from 9.2% to 15.3%). |
| In the protocol the following definition was used for orthodontic interventions: Steegmans et al. (2019a): 'Orthodontic interventions refer to the use of any type of orthodontic appliance that are used to move teeth or change the jaw size or position for orthodontic purposes. These interventions also include appliances to maintain or stabilize the results of orthodontic treatment, for example retainers.' | This definition was changed to: 'Orthodontic interventions refer to the use of any type of orthodontic appliance to move teeth or change the jaw size or position for orthodontic purposes. These interventions also include appliances to maintain or stabilize the results of orthodontic treatment, for example retainers.'<br><br>Rationale for change: The modified definition is more accurate, but did not change the original meaning of the definition of orthodontic interventions |
| Inclusion of Dr. Nicola Di Girolama as an author | Dr. Di Girolamo was consulted for his assistance in statistical and methodological issues |

**Additional file 2B. Selected journals and their 2018 impact factor (Clarivate Analytics 2021)**

| Journal | Impact factor |
|---|---|
| Cochrane Database of Systematic reviews | 7.755 |
| American Journal of Orthodontics and Dentofacial Orthopedics | 1.911 |
| European Journal of Orthodontics | 1.841 |
| Korean Journal of Orthodontics | 1.476 |
| Orthodontics and Craniofacial Research | 0.946 |

**Additional file 2C. Data collection forms***

| Items for the main manuscript | Description |
|---|---|
| Journal | List the pertinent journal |
| Year | Year of publication |
| Binder page number | List the binder page number |
| Reference | List full reference (Authors, Title, Journal) |
| Is the article a systematic review? | Answer: Yes/No<br>Consider definition of a systematic review |
| Is the systematic review eligible? | Answer: Yes/No<br>Consult the eligibility criteria for addressing this answer. |
| What was the orthodontic intervention? | List the type of orthodontic intervention. |
| Was seeking of adverse effects of interventions defined as a research objective of the review? | Answer: Yes/No<br>Yes: When seeking of adverse effects of interventions was defined as a research objective or as a research question or when adverse effects were predefined a priori as outcomes to assess.<br>No: Seeking of adverse effects of interventions was not defined as a research objective or as a research question or when adverse effects were not predefined a priori as outcomes to assess. |
| What adverse effects of interventions were defined as research objectives? | Answer: List adverse effects/NA<br>List all adverse effects of interventions that the reviewers defined as research objectives.<br>NA: When the following question was answered with a 'No': 'Was seeking of adverse effects of interventions defined as a research objective of the review?' |
| Did the review seek any findings related to adverse effects of interventions in the included studies? | Answer: Yes/No<br>Yes: Any findings related to adverse effects of interventions in the included studies were sought by the reviewers.<br>Seeking any findings related to adverse effects of interventions in the included studies refers to reporting anywhere in the review (except in the Abstract) that such adverse effects in the included studies were sought.<br>Yes: Yes is also scored when reviewers only reported findings related to adverse effects of interventions in the included studies, but did not report that they actually sought them or planned to seek them. For example 'Yes' will be scored when outcomes on adverse effects of interventions in the included studies were reported in the review, but were not defined as objectives of the review.<br>Yes: Yes is also scored when the reviewers reported that they planned to seek (for example in the research objectives) findings related to adverse effects of interventions in the included studies, but did not report on these findings. |

| | |
|---|---|
| | No: Findings related to adverse effects of interventions in the included studies were not sought by the reviewers. |
| Did the review report findings related to adverse effects of interventions sought in the included studies? | Answer: Yes/No<br>Yes: The review reported findings related to adverse effects of interventions sought in the included studies. 'Yes' is also scored when the review reported that no findings on adverse effects of interventions in the included studies were identified.<br>No: The review did not report any findings related to adverse effects of interventions sought in the included studies. |
| What findings related to adverse effects of interventions sought in the included studies were reported in the review? | Answer: List of adverse effects<br>List all findings related to adverse effect(s) of interventions that were identified in the included studies and reported in the review. |
| Rationale for assigning an effect as 'adverse' or 'not adverse' (In case of additional or ambivalent adverse effects) | Answer: Present the rationale for assigning an effect as 'adverse' or 'not adverse' (In case of additional or ambivalent adverse effects) |
| Were potential adverse effects of the intervention considered, discussed (weighed) anywhere in the review? | Answer: Yes/No<br>Yes: Potential adverse effect(s) of interventions in the included studies were sought and reported by the reviewers. 'Yes' is also scored when potential adverse effect(s) of interventions were not sought, but only considered, discussed (weighed) anywhere (except in the Abstract) in the review.<br>'No' is scored when potential adverse effects of the intervention were not considered, discussed (weighed) anywhere in the review. |
| Rationale for assigning an effect as 'adverse' or 'not adverse' (In case of additional or ambivalent adverse effects) | Answer: Present the rationale |

*To address our research question we will not consider what was reported regarding this question in the abstract and in the protocol of the review.

**Additional file 2D. Adverse effects hypothetically linked to orthodontic interventions according to Preoteasa et al. (2012)***

| **Local adverse effects** | |
|---|---|
| **Subgroup** | **Description** |
| Dental | • crown: decalcifications, decays, tooth wear, enamel cracks and fractures; discolorations, deterioration of prosthetic crown (as fracturing a ceramic one during debonding);<br>• root: root resorption, early closure of root apex, ankylosis;<br>• pulp: ischemia, pulpitis, necrosis; |
| Periodontal | • gingivitis, periodontitis, gingival recession or hypertrophy, alveolar bone loss, dehiscences, fenestrations, interdental fold, dark triangles; |
| Temporomandibular joint | • condylar resorption, temporomandibular dysfunction; |
| Soft tissues of the oral and maxillofacial region | • trauma (e.g., long archwires, headgear related), mucosal ulcerations or hyperplasia, chemical burns (e.g., etching related), thermal injuries (e.g., overheated burs), stomatitis, clumsy handling of dental instruments; |
| Unsatisfactory treatment outcome | • inadequate morpho-functional, aesthetic or functional final result, relapse, failure to complete treatment due to treatment dropout. |
| **Systemic adverse effects** | |
| **Subgroup** | **Description** |
| Psychological | • teasing, behavioral changes of patients and parents; discomfort associated with pain presence and aesthetic look discontents during orthodontic appliance usage; |
| Gastro-intestinal | • accidental swallowing of small parts of the orthodontic device (tubes, brackets); |
| Allergies | • to nickel or latex; |
| Cardiac | • infective endocarditis; |
| Chronic fatigue syndrome | |
| Cross infections | • from doctor to patient, patient to doctor, patient to patient. |

*Permission to reproduce this table was obtained on August 16 2018 from InTech's Publishing Ethics and Legal Affairs Department.

**Additional file 2E. Adverse effects hypothetically linked to orthodontic interventions***

| Adverse effects related to | Description |
|---|---|
| Tooth structures | Tooth crown<br>• decalcifications, decays, tooth wear, enamel cracks and fractures; discolorations, deterioration of prosthetic crown (as fracturing a ceramic one during debonding);<br>• iatrogenic damage to the crown, e.g., fracture as a result of trauma<br>Tooth root<br>• root resorption, early closure of root apex, ankylosis;<br>• iatrogenic damage to the root, e.g., fracture as a result of trauma<br>Tooth pulp<br>• ischemia, pulpitis, necrosis<br>• iatrogenic damage to the pulp, e.g., fracture as a result of trauma |
| Periodontal tissues | • gingivitis, periodontitis, gingival recession or hypertrophy, alveolar bone loss, dehiscences, fenestrations, interdental fold, dark triangles; tooth mobility, plague retention, bacterial count |
| Intraoral (non-tooth or periodontal) tissues | • intraoral tissue irritations and inflammation such as mucosal ulcerations or hyperplasia or irritations of the tongue (as a result of trauma by appliances, e.g., breakage, failure, loosening etc. of appliances or long arch wires)<br>• Scar formation after suturing<br>• chemical burns (e.g., etching related)<br>• thermal injuries (e.g., overheated burs)<br>• nerve damage<br>• tooth eruption, i.e., eruption disturbances (e.g., impactions) caused by orthodontic appliances |
| Extraoral tissues (non-temporomandibular tissues) | • cutting of lips or cheeks, eye injury (e.g., as a result of trauma by appliances, e.g., breakage, failure, loosening etc. of appliances or long arch wires or headgear-related trauma)<br>• discomfort on the lip |
| Temporomandibular tissues and disorders | • temporomandibular tissues and disorders |
| Appliance failure | • breakage, failure, loosening etc. of appliances<br>• long archwires, headgear-related trauma |
| Undesired treatment results | • inadequate morpho-functional, aesthetic or functional final result<br>• inaccuracy of the treatment result<br>• non predictability of the treatment result<br>• Dental side effects e.g., unwanted tipping of teeth, anchorage loss etc.<br>• Skeletal side effects, e.g., unwanted backward rotation of the mandible |
| Relapse and stability | • Relapse and stability of the obtained treatment result |
| Undesired qualitative experiences by the patient or carer(s) | Pain and discomfort<br>• orthodontic tooth movement-related pain and discomfort<br>• appliance (intervention)-related pain and discomfort: i.e., pain and discomfort as a result of the appliance (intervention) itself with or without pain and discomfort associated with tooth movement e.g., tension or pressure of the appliances (constriction of appliances), speech difficulties, eating difficulties, swallowing difficulties, food accumulation, bad tastes and smells<br>• additional intervention-related pain and discomfort, e.g., surgical and non-surgical adjunctive interventions to accelerate tooth movement |

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| | Tolerability/acceptance/stress issues with the treatment procedures<br>• Absence from work or studies and difficulties in daily activities<br>• collaboration (compliance) issues or failure to complete treatment, e.g., dropout<br>• patient anxiety<br>• being teased<br>• social discomfort<br>• embarrassment to wear the appliance<br>• behavioral changes of patients and parents, impaired family relationships<br>• aesthetic look discontents during orthodontic appliance usage<br>• concentration difficulties<br>• reduced enjoyment of food and change in taste<br>• sleeping difficulties<br>• removal of appliance during sleep<br>• development of mannerisms<br>Satisfaction with the treatment procedures and final result<br>• not satisfied with the treatment procedures (Check in text what was measured, i.e., during or after)<br>• not satisfied with the final treatment result (Check in text what was measured, i.e., during or after) |
| Gastro-intestinal | • accidental swallowing parts of the orthodontic device (tubes, brackets); |
| Allergy | • Allergies to nickel or latex; |
| Cardio | • infective endocarditis; |
| Chronic fatigue | |
| Cross infections | • from doctor to patient, patient to doctor, patient to patient. |
| Non-defined | Adverse effects that were not defined by the authors of the review: referring to 'any adverse effect', 'any side effect' etc. |
| Additional adverse effects | Additional adverse effects that were identified during data extraction that could not be labeled under any of the categories of adverse effects given in this table |

*Modified from Preoteasa et al. (Preoteasa 2012)

## References for additional file 2


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**Preoteasa 2012**
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**Additional file 3. Included reviews**

## Included systematic reviews of orthodontic interventions

| Journal* | Year | Reference |
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| AO | 2009 | Gordon JM, Rosenblatt M, Witmans M, Carey JP, Heo G, Major PW, Flores-Mir C. Rapid palatal expansion effects on nasal airway dimensions as measured by acoustic rhinometry. A systematic review. Angle Orthod. 2009 Sep;79(5):1000-7. doi: 10.2319/082108-441.1. |
| KJO | 2020 | Giudice AL, Spinuzza P, Rustico L, Messina G, Nucera R. Short-term treatment effects produced by rapid maxillary expansion evaluated with computed tomography: A |

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| | | systematic review with meta-analysis. Korean J Orthod. 2020 Sep 25;50(5):314-323. doi: 10.4041/kjod.2020.50.5.314. PMID: 32938824; PMCID: PMC7500570. |
| KJO | 2019 | Galan-Lopez L, Barcia-Gonzalez J, Plasencia E. A systematic review of the accuracy and efficiency of dental movements with Invisalign. Korean J Orthod. 2019 May;49(3):140-149. doi: 10.4041/kjod.2019.49.3.140. Epub 2019 May 21. |
| KJO | 2018 | Viwattanatipa N, Charnchairerk S. The effectiveness of corticotomy and piezocision on canine retraction: A systematic review.Korean J Orthod. 2018 May;48(3):200-211. doi: 10.4041/kjod.2018.48.3.200. |
| O&CR | 2021 | Bayome M, Park JH, Bay C, Kook YA. Distalization of maxillary molars using temporary skeletal anchorage devices: A systematic review and meta-analysis. Orthod Craniofac Res. 2021 Mar;24 Suppl 1:103-112. doi: 10.1111/ocr.12470. Epub 2021 Feb 8. |
| O&CR | 2021 | Arvind P TR, Jain RK. Skeletally anchored forsus fatigue resistant device for correction of Class II malocclusions-A systematic review and meta-analysis. Orthod Craniofac Res. 2021 Feb;24(1):52-61. doi: 10.1111/ocr.12414. Epub 2020 Sep 7. PMID: 32772479. |
| O&CR | 2021 | MacDonald, L., Zanjir, M., Laghapour Lighvan, N., da Costa, B. R., Suri, S., & Azarpazhooh, A. (2020). Efficacy and Safety of Different Interventions to Accelerate Maxillary Canine Retraction Following Premolar Extraction: A Systematic Review and Network Meta-analysis. Orthodontics & Craniofacial Research. doi:10.1111/ocr.12409 |
| O&CR | 2020 | Santana LG, Avelar K, Flores-Mir C, Marques LS. Incremental or maximal mandibular advancement in the treatment of class II malocclusion through functional appliances: A systematic review with meta-analysis. Orthod Craniofac Res. 2020 Nov;23(4):371-384. doi: 10.1111/ocr.12388. Epub 2020 May 29. PMID: 32390332. |
| O&CR | 2020 | Zhang B, Huang X, Huo S, Zhang C, Zhao S, Cen X, Zhao Z. Effect of clear aligners on oral health-related quality of life: A systematic review. Orthod Craniofac Res. 2020 Nov;23(4):363-370. doi: 10.1111/ocr.12382. Epub 2020 May 13. PMID: 32340082. |
| O&CR | 2020 | Niu X, Di Carlo G, Cornelis MA, Cattaneo PM. Three-dimensional analyses of short- and long-term effects of rapid maxillary expansion on nasal cavity and upper airway: A systematic review and meta-analysis. Orthod Craniofac Res. 2020 Aug;23(3):250-276. doi: 10.1111/ocr.12378. Epub 2020 May 5. PMID: 32248642. |
| O&CR | 2020 | Robertson L, Kaur H, Fagundes NCF, Romanyk D, Major P, Flores Mir C. Effectiveness of clear aligner therapy for orthodontic treatment: A systematic review. Orthod Craniofac Res. 2020 May;23(2):133-142. doi: 10.1111/ocr.12353. Epub 2019 Nov 13. PMID: 31651082. |
| O&CR | 2019 | Dab S, Chen K, Flores-Mir C. Short- and long-term potential effects of accelerated osteogenic orthodontic treatment: A systematic review and meta-analysis. Orthod Craniofac Res. 2019 May;22(2):61-68. doi: 10.1111/ocr.12272. Epub 2019 Mar 18. |
| O&CR | 2018 | Lee WC, Tu YK2, Huang CS, Chen R, Fu MW, Fu E. Pharyngeal airway changes following maxillary expansion or protraction: A meta-analysis.Orthod Craniofac Res. 2018 Feb;21(1):4-11. doi: 10.1111/ocr.12208. |
| O&CR | 2018 | Mohammed H, Rizk MZ, Wafaie K, Almuzian M. Effectiveness of nickel-titanium springs vs elastomeric chains in orthodontic space closure: A systematic review and meta-analysis.Orthod Craniofac Res. 2018 Feb;21(1):12-19. doi: 10.1111/ocr.12210. |
| O&CR | 2018 | Koletsi D, Makou M, Pandis N. Effect of orthodontic management and orofacial muscle training protocols on the correction of myofunctional and myoskeletal problems in developing dentition. A systematic review and meta-analysis.Orthod Craniofac Res. 2018 Nov;21(4):202-215. doi: 10.1111/ocr.12240. |
| O&CR | 2017 | Zheng M, Liu R, Ni Z, Yu Z. Efficiency, effectiveness and treatment stability of clear aligners: A systematic review and meta-analysis. Orthod Craniofac Res. 2017 Aug;20(3):127-133. doi: 10.1111/ocr.12177. |
| O&CR | 2014 | Cordasco G, Matarese G, Rustico L, Fastuca S, Caprioglio A, Lindauer SJ, Nucera R. Efficacy of orthopedic treatment with protraction facemask on skeletal Class III malocclusion: a systematic review and meta-analysis. Orthod Craniofac Res. 2014 Aug;17(3):133-43. doi: 10.1111/ocr.12040. |
| O&CR | 2014 | Papageorgiou SN, Konstantinidis I, Papadopoulou K, Jäger A, Bourauel C. A systematic review and meta-analysis of experimental clinical evidence on initial aligning archwires |

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| | | and archwire sequences. Orthod Craniofac Res. 2014 Nov;17(4):197-215. doi: 10.1111/ocr.12048. |

*Description of the abbreviated journals:
Cochrane library: Cochrane Database of Systematic Reviews
AJODO: American Journal of Orthodontics and Dentofacial Orthopedics
EJO: European Journal of Orthodontics
AO: Angle Orthodontist
KJO: Korean Journal of Orthodontics
O&CR: Orthodontics and Craniofacial Research

**Additional file 4. Excluded studies**

**Update**

The following reference from 2017: Arora A, Khattri S, Ismail NM, Kumbargere Nagraj S, Prashanti E. School dental screening programmes for oral health.Cochrane Database Syst Rev. 2017 Dec 21;12:CD012595. doi: 10.1002/14651858.CD012595.pub2. was excluded prior to title and abstract screening, because it was an update of the following reference by the same authors in 2019: Arora A, Khattri S, Ismail NM, Kumbargere Nagraj S, Eachempati P. School dental screening programmes for oral health. Cochrane Database Syst Rev. 2019 Aug 8;8:CD012595. doi: 10.1002/14651858.CD012595.pub3.

**Rationale for exclusion of studies**

A total of 180 studies were excluded during the title and abstract screening and 45 were excluded during full text screening. The rationales for exclusion were given for each study. Only one rationale was given per study even when more than one rationales could have been applied.

Rationales for exclusion of studies:

- Assessed exclusively adverse effects
- Not an orthodontic intervention
- Not the effects of orthodontic interventions were assessed
- Empty review
- review was later updated
- Review of animal studies
- Review of laboratory studies
- Review included orthognathic surgical interventions
- Assessed exclusively patients with congenital anomalies
- Review did not assess the effect of a specific type of intervention(s), but assessed an undefined orthodontic intervention, e.g., orthodontic treatment as a whole
- Review was conducted by one operator only
- The review is about a specific outcome of an intervention, which is ambiguous and could also be an adverse effect
- A Bayesian network meta-analysis was used

**Excluded studies during the title and abstract screening (n=180) with the rationale for exclusion**

| Journal* | Year | Reference | Rationale for exclusion |
|---|---|---|---|
| 1. Cochrane library | 2019 | Mulimani P, Abas AB, Karanth L, Colombatti R, Kulkarni P. Treatment of dental and orthodontic complications in thalassaemia. Cochrane Database Syst Rev. 2019 Aug 2;8:CD012969. doi: 10.1002/14651858.CD012969.pub2. | assessed exclusively adverse effects |
| 2. Cochrane library | 2019 | Arora A, Khattri S, Ismail NM, Kumbargere Nagraj S, Eachempati P. School dental screening programmes for oral health. Cochrane Database Syst Rev. 2019 Aug 8;8:CD012595. doi: 10.1002/14651858.CD012595.pub3. | not the effects of orthodontic interventions were assessed |
| 3. Cochrane library | 2018 | Millett DT, Cunningham SJ, O'Brien KD, Benson PE, de Oliveira CM. Orthodontic treatment for deep bite and retroclined upper front teeth in children.Cochrane Database Syst Rev. 2018 Feb 1;2:CD005972. doi: 10.1002/14651858.CD005972.pub4. | empty review |
| 4. Cochrane library | 2018 | Mandall NA, Hickman J, Macfarlane TV, Mattick RC, Millett DT, Worthington HV. Adhesives for fixed orthodontic brackets.Cochrane Database Syst Rev. 2018 Apr 9;4:CD002282. doi: 10.1002/14651858.CD002282.pub2. | not the effects of orthodontic interventions were assessed |
| 5. Cochrane library | 2017 | Millett DT, Mandall NA, Mattick RC, Hickman J, Glenny AM. Adhesives for bonded molar tubes during fixed brace treatment. Cochrane Database Syst Rev. 2017 Feb 23;2:CD008236. doi: 10.1002/14651858.CD008236.pub3. | not the effects of orthodontic interventions were assessed |
| 6. Cochrane library | 2017 | Agnihotry A, Fedorowicz Z, Nasser M, Gill KS. Resorbable versus titanium plates for orthognathic surgery.Cochrane Database Syst Rev. 2017 Oct 4;10:CD006204. doi: 10.1002/14651858.CD006204.pub3. | not the effects of orthodontic interventions were assessed |
| 7. Cochrane library | 2017 | Monk AB, Harrison JE, Worthington HV, Teague A. Pharmacological interventions for pain relief during orthodontic treatment. Cochrane Database Syst Rev. 2017 Nov 28;11:CD003976. doi: 10.1002/14651858.CD003976.pub2. | not the effects of orthodontic interventions were assessed |
| 8. Cochrane library | 2016 | Ashley PF, Parekh S, Moles DR, Anand P, MacDonald LC. Preoperative analgesics for additional pain relief in children and adolescents having dental treatment. Cochrane Database Syst Rev. 2016 Aug 8;(8):CD008392. doi: 10.1002/14651858.CD008392.pub3. | not the effects of orthodontic interventions were assessed |
| 9. Cochrane library | 2016 | Ghaeminia H, Perry J, Nienhuijs ME, Toedtling V, Tummers M, Hoppenreijs TJ, Van der Sanden WJ, Mettes TG. Surgical removal versus retention for the management of asymptomatic disease-free impacted wisdom teeth. Cochrane Database Syst Rev. 2016 Aug 31;(8):CD003879. doi: 10.1002/14651858.CD003879.pub4. | not the effects of orthodontic interventions were assessed |
| 10. Cochrane library | 2016 | Carvalho FR, Lentini-Oliveira DA, Prado LB, Prado GF, Carvalho LB. Oral appliances and functional | not the effects of orthodontic |

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| | | orthopaedic appliances for obstructive sleep apnoea in children. Cochrane Database Syst Rev. 2016 Oct 5;10:CD005520. | interventions were assessed |
| 11. Cochrane library | 2016 | Millett DT, Glenny AM, Mattick RC, Hickman J, Mandall NA. Adhesives for fixed orthodontic bands. Cochrane Database Syst Rev. 2016 Oct 25;10:CD004485. | not the effects of orthodontic interventions were assessed |
| 12. Cochrane library | 2016 | Fleming PS, Strydom H, Katsaros C, MacDonald L, Curatolo M, Fudalej P, Pandis N. Non-pharmacological interventions for alleviating pain during orthodontic treatment. Cochrane Database Syst Rev. 2016 Dec 23;12:CD010263. doi: 10.1002/14651858.CD010263.pub2. | not the effects of orthodontic interventions were assessed |
| 13. Cochrane library | 2015 | Ahangari Z, Nasser M, Mahdian M, Fedorowicz Z, Marchesan MA. Interventions for the management of external root resorption. Cochrane Database Syst Rev. 2015 Nov 24;(11):CD008003. doi: 10.1002/14651858.CD008003.pub3.(discuss met Reint: moeten we deze wel includeren) | assessed exclusively adverse effects |
| 14. Cochrane library | 2013 | Belmonte FM, Macedo CR, Day PF, Saconato H, Fernandes Moça Trevisani V. Interventions for treating traumatised permanent front teeth: luxated (dislodged) teeth.Cochrane Database Syst Rev. 2013 Apr 30;(4):CD006203. doi: 10.1002/14651858.CD006203.pub2. | empty review |
| 15. Cochrane library | 2013 | Yu Y, Sun J, Lai W, Wu T, Koshy S, Shi Z. Interventions for managing relapse of the lower front teeth after orthodontic treatment. Cochrane Database Syst Rev. 2013 Sep 6;(9):CD008734. doi: 10.1002/14651858.CD008734.pub2. | empty review |
| 16. Cochrane library | 2013 | Hu H, Li C, Li F, Chen J, Sun J, Zou S, Sandham A, Xu Q, Riley P, Ye Q. Enamel etching for bonding fixed orthodontic braces. Cochrane Database Syst Rev. 2013 Nov 25;(11):CD005516. doi: 10.1002/14651858.CD005516.pub2. | not the effects of orthodontic interventions were assessed |
| 17. Cochrane library | 2013 | Benson PE, Parkin N, Dyer F, Millett DT, Furness S, Germain P. Fluorides for the prevention of early tooth decay (demineralised white lesions) during fixed brace treatment. Cochrane Database Syst Rev. 2013 Dec 12;(12):CD003809. doi: 10.1002/14651858.CD003809.pub3. | not the effects of orthodontic interventions were assessed |
| 18. EJO | 2021 | Alrashed M, Alqerban A. The relationship between malocclusion and oral health-related quality of life among adolescents: a systematic literature review and meta-analysis. Eur J Orthod. 2021 Apr 3;43(2):173-183. doi: 10.1093/ejo/cjaa051. PMID: 33009547. | not the effects of orthodontic interventions were assessed |
| 19. EJO | 2021 | Mulier D, Gaitán Romero L, Führer A, Martin C, Shujaat S, Shaheen E, Politis C, Jacobs R. Long-term dental stability after orthognathic surgery: a systematic review. Eur J Orthod. 2021 Jan 29;43(1):104-112. doi: 10.1093/ejo/cjaa022. PMID: 32901268. | review included orthognathic surgical interventions |
| 20. EJO | 2021 | Palikaraki G, Makrygiannakis MA, Zafeiriadis AA, Benetou V, Sanoudos M, Bitsanis I, Tsolakis AI. The effect of facemask in patients with unilateral cleft | assessed exclusively patients with |

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| | | lip and palate: a systematic review and meta-analysis. Eur J Orthod. 2021 Jan 29;43(1):69-79. doi: 10.1093/ejo/cjaa027. PMID: 32274494. | congenital anomalies |
| 21. EJO | 2021 | Gandhi V, Mehta S, Gauthier M, Mu J, Kuo CL, Nanda R, Yadav S. Comparison of external apical root resorption with clear aligners and pre-adjusted edgewise appliances in non-extraction cases: a systematic review and meta-analysis. Eur J Orthod. 2021 Jan 29;43(1):15-24. doi: 10.1093/ejo/cjaa013. PMID: 32077935; PMCID: PMC7846172. | assessed exclusively adverse effects |
| 22. EJO | 2020 | Stucki S, Gkantidis N. Assessment of techniques used for superimposition of maxillary and mandibular 3D surface models to evaluate tooth movement: a systematic review. Eur J Orthod. 2020 Nov 3;42(5):559-570. doi: 10.1093/ejo/cjz075. PMID: 31742598. | not an orthodontic intervention |
| 23. EJO | 2020 | Rodrigues AS, Antunes LS, Pinheiro LHM, Guimarães LS, Calansans-Maia JA, Küchler EC, Antunes LAA. Is dental agenesis associated with craniofacial morphology pattern? A systematic review and meta-analysis. Eur J Orthod. 2020 Nov 3;42(5):534-543. doi: 10.1093/ejo/cjz087. PMID: 31783403. | not an orthodontic intervention |
| 24. EJO | 2020 | Kaklamanos EG, Makrygiannakis MA, Athanasiou AE. Does medication administration affect the rate of orthodontic tooth movement and root resorption development in humans? A systematic review. Eur J Orthod. 2020 Sep 11;42(4):407-414. doi: 10.1093/ejo/cjz063. PMID: 31421637. | not the effects of orthodontic interventions were assessed |
| 25. EJO | 2020 | de Araujo CM, Schroder AGD, de Araujo BMM, Cavalcante-Leão BL, Stechman-Neto J, Zeigelboim BS, Santos RS, Guariza-Filho O. Impact of orthodontic-surgical treatment on quality of life: a meta-analysis. Eur J Orthod. 2020 Jun 23;42(3):281-289. doi: 10.1093/ejo/cjz093. PMID: 31784741. | review included orthognathic surgical interventions |
| 26. EJO | 2020 | Papadimitriou A, Kakali L, Pazera P, Doulis I, Kloukos D. Social media and orthodontic treatment from the patient's perspective: a systematic review. Eur J Orthod. 2020 Jun 23;42(3):231-241. doi: 10.1093/ejo/cjz029. PMID: 31107943. | not the effects of orthodontic interventions were assessed |
| 27. EJO | 2020 | Zymperdikas VF, Yavropoulou MP, Kaklamanos EG, Papadopoulos MA. Effects of systematic bisphosphonate use in patients under orthodontic treatment: a systematic review. Eur J Orthod. 2020 Jan 27;42(1):60-71. doi: 10.1093/ejo/cjz021. PMID: 31009953. | not an orthodontic intervention |
| 28. EJO | 2019 | Sardana D, Manchanda S, Ekambaram M, Yang Y, McGrath CP, Yiu CKY. Effectiveness of self-applied topical fluorides against enamel white spot lesions from multi-bracketed fixed orthodontic treatment: a systematic review. Eur J Orthod. 2019 Nov 15;41(6):661-668. doi: 10.1093/ejo/cjz015. Erratum in: Eur J Orthod. 2019 Nov 15;41(6):669. PMID: 31112229. | not an orthodontic intervention |
| 29. EJO | 2019 | Makrygiannakis MA, Kaklamanos EG, Athanasiou AE. Does long-term use of pain relievers have an impact on the rate of orthodontic tooth | review of animal studies |

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| | | movement? A systematic review of animal studies. Eur J Orthod. 2019 Sep 21;41(5):468-477. doi: 10.1093/ejo/cjy079. PMID: 30590549. | |
| 30. EJO | 2019 | Kakali L, Alharbi M, Pandis N, Gkantidis N, Kloukos D. Success of palatal implants or mini-screws placed median or paramedian for the reinforcement of anchorage during orthodontic treatment: a systematic review. Eur J Orthod. 2019 Jan 23;41(1):9-20. doi: 10.1093/ejo/cjy015. | not the effects of orthodontic interventions were assessed |
| 31. EJO | 2019 | Samandara A, Papageorgiou SN, Ioannidou-Marathiotou I, Kavvadia-Tsatala S, Papadopoulos MA. Evaluation of orthodontically induced external root resorption following orthodontic treatment using cone beam computed tomography (CBCT): a systematic review and meta-analysis. Eur J Orthod. 2019 Jan 23;41(1):67-79. doi: 10.1093/ejo/cjy027. | assessed exclusively adverse effects |
| 32. EJO | 2019 | Bartolucci ML, Bortolotti F, Martina S2, Corazza G, Michelotti A, Alessandri-Bonetti G. Dental and skeletal long-term side effects of mandibular advancement devices in obstructive sleep apnea patients: a systematic review with meta-regression analysis. Eur J Orthod. 2019 Jan 23;41(1):89-100. doi: 10.1093/ejo/cjy036. | not the effects of orthodontic interventions were assessed |
| 33. EJO | 2019 | Mohammed H, Rizk MZ, Wafaie K, Ulhaq A, Almuzian M. Reminders improve oral hygiene and adherence to appointments in orthodontic patients: a systematic review and meta-analysis. Eur J Orthod. 2019 Mar 29;41(2):204-213. doi: 10.1093/ejo/cjy045. | not the effects of orthodontic interventions were assessed |
| 34. EJO | 2019 | Makrygiannakis MA, Kaklamanos EG, Athanasiou AE. Effects of systemic medication on root resorption associated with orthodontic tooth movement: a systematic review of animal studies. Eur J Orthod. 2019 Aug 8;41(4):346-359. doi: 10.1093/ejo/cjy048. | review of animal studies |
| 35. EJO | 2019 | De Grauwe A, Ayaz I, Shujaat S, Dimitrov S, Gbadegbegnon L, Vande Vannet B, Jacobs R. CBCT in orthodontics: a systematic review on justification of CBCT in a paediatric population prior to orthodontic treatment. Eur J Orthod. 2019 Aug 8;41(4):381-389. doi: 10.1093/ejo/cjy066. | not the effects of orthodontic interventions were assessed |
| 36. EJO | 2018 | Chen J, Wan J, You L. Speech and orthodontic appliances: a systematic literature review.Eur J Orthod. 2018 Jan 23;40(1):29-36. doi: 10.1093/ejo/cjx023. | assessed exclusively adverse effects |
| 37. EJO | 2018 | Alyammahi AS, Kaklamanos EG, Athanasiou AE. Effectiveness of extraction of primary canines for interceptive management of palatally displaced permanent canines: a systematic review and meta-analysis.Eur J Orthod. 2018 Apr 6;40(2):149-156. doi: 10.1093/ejo/cjx042. | not the effects of orthodontic interventions were assessed |
| 38. EJO | 2018 | Lo Giudice A, Barbato E, Cosentino L, Ferraro CM, Leonardi R Alveolar bone changes after rapid maxillary expansion with tooth-born appliances: a | assessed exclusively adverse effects |

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| | | systematic review.Eur J Orthod. 2018 May 25;40(3):296-303. doi: 10.1093/ejo/cjx057. | |
| 39. EJO | 2018 | Haugland L, Kristensen KD, Lie SA, Vandevska-Radunovic V. The effect of biologic factors and adjunctive therapies on orthodontically induced inflammatory root resorption: a systematic review and meta-analysis.Eur J Orthod. 2018 May 25;40(3):326-336. doi: 10.1093/ejo/cjy003. | assessed exclusively adverse effects |
| 40. EJO | 2018 | Alharbi F, Almuzian M, Bearn D. Miniscrews failure rate in orthodontics: systematic review and meta-analysis.Eur J Orthod. 2018 Sep 28;40(5):519-530. doi: 10.1093/ejo/cjx093. | assessed exclusively adverse effects |
| 41. EJO | 2018 | Grisar K, Chaabouni D, Romero LPG, Vandendriessche T, Politis C, Jacobs R. Autogenous transalveolar transplantation of maxillary canines: a systematic review and meta-analysis.Eur J Orthod. 2018 Nov 30;40(6):608-616. doi: 10.1093/ejo/cjy026. | not an orthodontic intervention |
| 42. EJO | 2018 | Dumbryte I, Vebriene J, Linkeviciene L, Malinauskas M. Enamel microcracks in the form of tooth damage during orthodontic debonding: a systematic review and meta-analysis of in vitro studies.Eur J Orthod. 2018 Nov 30;40(6):636-648. doi: 10.1093/ejo/cjx102. | review of laboratory studies |
| 43. EJO | 2018 | Makrygiannakis MA, Kaklamanos EG, Athanasiou AE. Does common prescription medication affect the rate of orthodontic tooth movement? A systematic review.Eur J Orthod. 2018 Nov 30;40(6):649-659. doi: 10.1093/ejo/cjy001. | review of animal studies |
| 44. EJO | 2017 | Castroflorio T, Bargellini A, Rossini G, Cugliari G, Deregibus A. Sleep bruxism in adolescents: a systematic literature review of related risk factors. Eur J Orthod. 2017 Feb;39(1):61-68. doi: 10.1093/ejo/cjw012. | not an orthodontic intervention |
| 45. EJO | 2017 | Höchli D, Hersberger-Zurfluh M, Papageorgiou SN, Eliades T. Interventions for orthodontically induced white spot lesions: a systematic review and meta-analysis. Eur J Orthod. 2017 Apr 1;39(2):122-133. doi: 10.1093/ejo/cjw065. | not an orthodontic intervention |
| 46. EJO | 2017 | Sonesson M, Bergstrand F, Gizani S, Twetman S. Management of post-orthodontic white spot lesions: an updated systematic review. Eur J Orthod. 2017 Apr 1;39(2):116-121. doi: 10.1093/ejo/cjw023. | not an orthodontic intervention |
| 47. EJO | 2017 | Dalessandri D, Parrini S, Rubiano R, Gallone D, Migliorati M. Impacted and transmigrant mandibular canines incidence, aetiology, and treatment: a systematic review. Eur J Orthod. 2017 Apr 1;39(2):161-169. doi: 10.1093/ejo/cjw027. | not an orthodontic intervention |
| 48. EJO | 2017 | Yi J, Ge M, Li M, Li C, Li Y, Li X, Zhao Z. Comparison of the success rate between self-drilling and self-tapping miniscrews: a systematic review and meta-analysis. Eur J Orthod. 2017 Jun 1;39(3):287-293. doi: 10.1093/ejo/cjw036. | not the effects of orthodontic interventions were assessed |

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| 49. EJO | 2017 | Mousoulea S, Kloukos D, Sampaziotis D, Vogiatzi T, Eliades T. Condylar resorption in orthognathic patients after mandibular bilateral sagittal split osteotomy: a systematic review. Eur J Orthod. 2017 Jun 1;39(3):294-309. doi: 10.1093/ejo/cjw045. | assessed exclusively adverse effects |
| 50. EJO | 2017 | Zimmerman JN, Lee J, Pliska BT. Reliability of upper pharyngeal airway assessment using dental CBCT: a systematic review. Eur J Orthod. 2017 Oct 1;39(5):489-496. doi: 10.1093/ejo/cjw079. | not an orthodontic intervention |
| 51. EJO | 2017 | Becking BE, Verweij JP, Kalf-Scholte SM, Valkenburg C, Bakker EWP, van Merkesteyn JPR. Impact of adenotonsillectomy on the dentofacial development of obstructed children: a systematic review and meta-analysis. Eur J Orthod. 2017 Oct 1;39(5):509-518. doi: 10.1093/ejo/cjx005. | not an orthodontic intervention |
| 52. EJO | 2017 | Sandhu SS, Piepho HP, Khehra HS. Comparing the effectiveness profile of pharmacological interventions used for orthodontic pain relief: an arm-based multilevel network meta-analysis of longitudinal data. Eur J Orthod. 2017 Nov 30;39(6):601-614. doi: 10.1093/ejo/cjw088. | not an orthodontic intervention |
| 53. EJO | 2016 | Rakhshan V, Rakhshan H. Meta-analysis and systematic review of the number of non-syndromic congenitally missing permanent teeth per affected individual and its influencing factors. Eur J Orthod. 2016 Apr;38(2):170-7. doi: 10.1093/ejo/cjv008. | not an orthodontic intervention |
| 54. EJO | 2016 | Goracci C, Franchi L, Vichi A, Ferrari M3. Accuracy, reliability, and efficiency of intraoral scanners for full-arch impressions: a systematic review of the clinical evidence. Eur J Orthod. 2016 Aug;38(4):422-8. doi: 10.1093/ejo/cjv077. | not an orthodontic intervention |
| 55. EJO | 2016 | Aragón ML, Pontes LF, Bichara LM, Flores-Mir C, Normando D. Validity and reliability of intraoral scanners compared to conventional gypsum models measurements: a systematic review. Eur J Orthod. 2016 Aug;38(4):429-34. doi: 10.1093/ejo/cjw033. (geen PDF) | not an orthodontic intervention |
| 56. EJO | 2016 | Iodice G, Danzi G, Cimino R, Paduano S, Michelotti A. Association between posterior crossbite, skeletal, and muscle asymmetry: a systematic review. Eur J Orthod. 2016 Dec;38(6):638-651. | not an orthodontic intervention |
| 57. EJO | 2015 | Dimberg L, Arnrup K, Bondemark L. The impact of malocclusion on the quality of life among children and adolescents: a systematic review of quantitative studies. Eur J Orthod. 2015 Jun;37(3):238-47. doi: 10.1093/ejo/cju046. | not an orthodontic intervention |
| 58. EJO | 2015 | Migliorati M, Isaia L, Cassaro A, Rivetti A, Silvestrini-Biavati F, Gastaldo L, Piccardo I, Dalessandri D, Silvestrini-Biavati A. Efficacy of professional hygiene and prophylaxis on preventing plaque increase in orthodontic patients with multibracket appliances: a systematic review. Eur J Orthod. 2015 Jun;37(3):297-307. doi: 10.1093/ejo/cju044. | not an orthodontic intervention |
| 59. EJO | 2015 | Nazarali N, Altalibi M, Nazarali S, Major MP, Flores-Mir C, Major PW. Mandibular advancement appliances for the treatment of paediatric | not an orthodontic intervention |

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| | | obstructive sleep apnea: a systematic review. Eur J Orthod. 2015 Dec;37(6):618-26. doi: 10.1093/ejo/cju101. | |
| 60. EJO | 2014 | Gomes Lde C, Horta KO, Gonçalves JR, Santos-Pinto AD. Systematic review: craniocervical posture and craniofacial morphology. Eur J Orthod. 2014 Feb;36(1):55-66. doi: 10.1093/ejo/cjt004. | not an orthodontic intervention |
| 61. EJO | 2014 | Dalessandri D, Salgarello S, Dalessandri M, Lazzaroni E, Piancino M, Paganelli C, Maiorana C, Santoro F. Determinants for success rates of temporary anchorage devices in orthodontics: a meta-analysis (n > 50). Eur J Orthod. 2014 Jun;36(3):303-13. doi: 10.1093/ejo/cjt049. | not the effects of orthodontic interventions were assessed |
| 62. EJO | 2014 | Kloukos D, Eliades T, Sculean A, Katsaros C. Indication and timing of soft tissue augmentation at maxillary and mandibular incisors in orthodontic patients. A systematic review.Eur J Orthod. 2014 Aug;36(4):442-9. doi: 10.1093/ejo/cjt073. | not an orthodontic intervention |
| 63. EJO | 2014 | Winsauer H, Vlachojannis C, Bumann A, Vlachojannis J, Chrubasik S. Paramedian vertical palatal bone height for mini-implant insertion: a systematic review. Eur J Orthod. 2014 Oct;36(5):541-9. doi: 10.1093/ejo/cjs068. | not an orthodontic intervention |
| 64. EJO | 2014 | Forst D, Nijjar S, Khaled Y, Lagravere M, Flores-Mir C. Radiographic assessment of external root resorption associated with jackscrew-based maxillary expansion therapies: a systematic review. Eur J Orthod. 2014 Oct;36(5):576-85. doi: 10.1093/ejo/cjt090. | assessed exclusively adverse effects |
| 65. EJO | 2013 | Livas C, Delli K. Subjective and objective perception of orthodontic treatment need: a systematic review.Eur J Orthod. 2013 Jun;35(3):347-53. doi: 10.1093/ejo/cjr142. | not an orthodontic intervention |
| 66. EJO | 2013 | Alves M Jr, Baratieri C, Mattos CT, Araújo MT, Maia LC. Root repair after contact with mini-implants: systematic review of the literature.Eur J Orthod. 2013 Aug;35(4):491-9. doi: 10.1093/ejo/cjs025. Epub 2012 Apr 26. | not an orthodontic intervention |
| 67. EJO | 2013 | Perinetti G, Primozic J, Manfredini D, Di Lenarda R, Contardo L. The diagnostic potential of static body-sway recording in orthodontics: a systematic review. Eur J Orthod. 2013 Oct;35(5):696-705. doi: 10.1093/ejo/cjs085. | not an orthodontic intervention |
| 68. EJO | 2013 | Iodice G, Danzi G, Cimino R, Paduano S, Michelotti A. Association between posterior crossbite, masticatory muscle pain, and disc displacement: a systematic review. Eur J Orthod. 2013 Dec;35(6):737-44. doi: 10.1093/ejo/cjt024. | not an orthodontic intervention |
| 69. EJO | 2013 | Altalibi M, Saltaji H, Edwards R, Major PW, Flores-Mir C. Indices to assess malocclusions in patients with cleft lip and palate. Eur J Orthod. 2013 Dec;35(6):772-82. doi: 10.1093/ejo/cjt009. | not an orthodontic intervention |
| 70. EJO | 2013 | Walker SL, Tieu LD, Flores-Mir C. Radiographic comparison of the extent of orthodontically induced external apical root resorption in vital and | assessed exclusively adverse effects |

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| | | root-filled teeth: a systematic review. Eur J Orthod. 2013 Dec;35(6):796-802. doi: 10.1093/ejo/cjs101. | |
| 71. EJO | 2011 | Fudalej P, Dragan M, Wedrychowska-Szulc B. Prediction of the outcome of orthodontic treatment of Class III malocclusions--a systematic review. Eur J Orthod. 2011 Apr;33(2):190-7. doi: 10.1093/ejo/cjq052. | not an orthodontic intervention |
| 72. EJO | 2011 | Ahrens A, McGrath C, Hägg U. A systematic review of the efficacy of oral appliance design in the management of obstructive sleep apnoea. Eur J Orthod. 2011 Jun;33(3):318-24. doi: 10.1093/ejo/cjq079. | not an orthodontic intervention |
| 73. AJODO | 2021 | Malekshoar M, Malekshoar M, Javanshir B. Challenges, limitations, and solutions for orthodontists during the coronavirus pandemic: A review. Am J Orthod Dentofacial Orthop. 2021 Jan;159(1):e59-e71. doi: 10.1016/j.ajodo.2020.09.009. Epub 2020 Oct 19. PMID: 33223376; PMCID: PMC7571895. | not the effects of orthodontic interventions were assessed |
| 74. AJODO | 2020 | Tepedino M, Cattaneo PM, Niu X, Cornelis MA. Interradicular sites and cortical bone thickness for miniscrew insertion: A systematic review with meta-analysis. Am J Orthod Dentofacial Orthop. 2020 Dec;158(6):783-798.e20. doi: 10.1016/j.ajodo.2020.05.011. Epub 2020 Oct 16. Erratum in: Am J Orthod Dentofacial Orthop. 2021 Jun;159(6):711. PMID: 33077369. | not the effects of orthodontic interventions were assessed |
| 75. AJODO | 2020 | ElShehaby M, Mofti B, Montasser MA, Bearn D. Powered vs manual tooth brushing in patients with fixed orthodontic appliances: A systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2020 Nov;158(5):639-649. doi: 10.1016/j.ajodo.2020.04.018. Epub 2020 Sep 17. PMID: 32951930. | not an orthodontic intervention |
| 76. AJODO | 2020 | Macey R, Thiruvenkatachari B, O'Brien K, Batista KBSL. Do malocclusion and orthodontic treatment impact oral health? A systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2020 Jun;157(6):738-744.e10. doi: 10.1016/j.ajodo.2020.01.015. PMID: 32487303. | review did not assess the effect of a specific type of intervention(s), but assessed an undefined orthodontic intervention, e.g., orthodontic treatment as a whole |
| 77. AJODO | 2020 | Arn ML, Dritsas K, Pandis N, Kloukos D. The effects of fixed orthodontic retainers on periodontal health: A systematic review. Am J Orthod Dentofacial Orthop. 2020 Feb;157(2):156-164.e17. doi: 10.1016/j.ajodo.2019.10.010. PMID: 32005466. | assessed exclusively adverse effects |
| 78. AJODO | 2019 | Vásquez-Cárdenas J, Zapata-Noreña Ó, Carvajal-Flórez Á, Barbosa-Liz DM, Giannakopoulos NN, Faggion CM Jr. Systematic reviews in orthodontics: Impact of the PRISMA for Abstracts checklist on completeness of reporting. Am J Orthod Dentofacial | not an orthodontic intervention |

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| | | Orthop. 2019 Oct;156(4):442-452.e12. doi: 10.1016/j.ajodo.2019.05.009. PMID: 31582116. | |
| 79. AJODO | 2019 | Barretto Dos Santos Lopes Batista K, Thiruvenkatachari B, O'Brien K. Intention-to-treat analysis: Are we managing dropouts and missing data properly in research on orthodontic treatment? A systematic review. Am J Orthod Dentofacial Orthop. 2019 Jan;155(1):19-27.e3. doi: 10.1016/j.ajodo.2018.08.013. | not an orthodontic intervention |
| 80. AJODO | 2019 | Currell SD, Liaw A, Blackmore Grant PD, Esterman A4, Nimmo A. Orthodontic mechanotherapies and their influence on external root resorption: A systematic review. Am J Orthod Dentofacial Orthop. 2019 Mar;155(3):313-329. doi: 10.1016/j.ajodo.2018.10.015. | assessed exclusively adverse effects |
| 81. AJODO | 2019 | Yi J, Lu W, Xiao J, Li X, Li Y, Zhao Z. Effect of conventional combined orthodontic-surgical treatment on oral health-related quality of life: A systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2019 Jul;156(1):29-43.e5. doi: 10.1016/j.ajodo.2019.03.008. | review included orthognathic surgical interventions |
| 82. AJODO | 2018 | Al-Jewair T, Stellrecht E, Lewandowski L, Chakaki R. American Association of Orthodontists Foundation Craniofacial Growth Legacy Collection in the orthodontic literature-use and trends: A systematic review.Am J Orthod Dentofacial Orthop. 2018 Jan;153(1):15-25.e10. doi: 10.1016/j.ajodo.2017.07.015. | not an orthodontic intervention |
| 83. AJODO | 2018 | Barber S, Bekker HL, Meads D, Pavitt S, Khambay B. Identification and appraisal of outcome measures used to evaluate hypodontia care: A systematic review.Am J Orthod Dentofacial Orthop. 2018 Feb;153(2):184-194.e18. doi: 10.1016/j.ajodo.2017.10.010. | not an orthodontic intervention |
| 84. AJODO | 2017 | Eslami E, Barkhordar H, Abramovitch K, Kim J, Masoud MI. Cone-beam computed tomography vs conventional radiography in visualization of maxillary impacted-canine localization: A systematic review of comparative studies. Am J Orthod Dentofacial Orthop. 2017 Feb;151(2):248-258. doi: 10.1016/j.ajodo.2016.07.018. | not an orthodontic intervention |
| 85. AJODO | 2017 | Al-Moghrabi D, Salazar FC, Pandis N, Fleming PS. Compliance with removable orthodontic appliances and adjuncts: A systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2017 Jul;152(1):17-32. doi: 10.1016/j.ajodo.2017.03.019. | not the effects of orthodontic interventions were assessed |
| 86. AJODO | 2017 | Al Makhmari SA, Kaklamanos EG, Athanasiou AE. Short-term and long-term effectiveness of powered toothbrushes in promoting periodontal health during orthodontic treatment: A systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2017 Dec;152(6):753-766.e7. doi: 10.1016/j.ajodo.2017.09.003. | not an orthodontic intervention |
| 87. AJODO | 2016 | Rossini G, Parrini S, Castroflorio T, Deregibus A, Debernardi CL. Diagnostic accuracy and measurement sensitivity of digital models for | not an orthodontic intervention |

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| | | orthodontic purposes: A systematic review. Am J Orthod Dentofacial Orthop. 2016 Feb;149(2):161-70. doi: 10.1016/j.ajodo.2015.06.029. | |
| 88. AJODO | 2016 | Peiró-Guijarro MA, Guijarro-Martínez R, Hernández-Alfaro F. Surgery first in orthognathic surgery: A systematic review of the literature. Am J Orthod Dentofacial Orthop. 2016 Apr;149(4):448-62. doi: 10.1016/j.ajodo.2015.09.022. | not an orthodontic intervention |
| 89. AJODO | 2016 | Incerti-Parenti S, Checchi V, Ippolito DR, Gracco A, Alessandri-Bonetti G. Periodontal status after surgical-orthodontic treatment of labially impacted canines with different surgical techniques: A systematic review. Am J Orthod Dentofacial Orthop. 2016 Apr;149(4):463-72. doi: 10.1016/j.ajodo.2015.10.019. | not an orthodontic intervention |
| 90. AJODO | 2016 | Ata-Ali F, Ata-Ali J, Ferrer-Molina M, Cobo T, De Carlos F, Cobo J. Adverse effects of lingual and buccal orthodontic techniques: A systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2016 Jun;149(6):820-9. doi: 10.1016/j.ajodo.2015.11.031. | assessed exclusively adverse effects |
| 91. AJODO | 2016 | Sandhu SS, Cheema MS, Khehra HS. Comparative effectiveness of pharmacologic and nonpharmacologic interventions for orthodontic pain relief at peak pain intensity: A Bayesian network meta-analysis. Am J Orthod Dentofacial Orthop. 2016 Jul;150(1):13-32. doi: 10.1016/j.ajodo.2015.12.025. | not an orthodontic intervention |
| 92. AJODO | 2016 | Cadenas-Perula M, Yañez-Vico RM, Solano-Reina E, Iglesias-Linares A. Effectiveness of biologic methods of inhibiting orthodontic tooth movement in animal studies. Am J Orthod Dentofacial Orthop. 2016 Jul;150(1):33-48. doi: 10.1016/j.ajodo.2016.01.015. | review of animal studies |
| 93. AJODO | 2016 | Parrini S, Rossini G, Castroflorio T, Fortini A, Deregibus A, Debernardi C. Laypeople's perceptions of frontal smile esthetics: A systematic review. Am J Orthod Dentofacial Orthop. 2016 Nov;150(5):740-750. doi: 10.1016/j.ajodo.2016.06.022. | not the effects of orthodontic interventions were assessed |
| 94. AJODO | 2015 | Roscoe MG, Meira JB, Cattaneo PM. Association of orthodontic force system and root resorption: A systematic review. Am J Orthod Dentofacial Orthop. 2015 May;147(5):610-26. doi: 10.1016/j.ajodo.2014.12.026. | assessed exclusively adverse effects |
| 95. AJODO | 2014 | Afrand M, Ling CP, Khosrotehrani S, Flores-Mir C, Lagravère-Vich MO. Anterior cranial-base time-related changes: A systematic review. Am J Orthod Dentofacial Orthop. 2014 Jul;146(1):21-32.e6. doi: 10.1016/j.ajodo.2014.03.019. | not an orthodontic intervention |
| 96. AJODO | 2014 | Tsichlaki A, O'Brien K. Do orthodontic research outcomes reflect patient values? A systematic review of randomized controlled trials involving children. Am J Orthod Dentofacial Orthop. 2014 Sep;146(3):279-85. doi: 10.1016/j.ajodo.2014.05.022. | not the effects of orthodontic interventions were assessed |

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| 97. AJODO | 2013 | Katyal V, Pamula Y, Martin AJ, Daynes CN, Kennedy JD, Sampson WJ. Craniofacial and upper airway morphology in pediatric sleep-disordered breathing: Systematic review and meta-analysis.Am J Orthod Dentofacial Orthop. 2013 Jan;143(1):20-30.e3. doi: 10.1016/j.ajodo.2012.08.021. | not an orthodontic intervention |
| 98. AJODO | 2013 | Chen H, Liu X, Dai J, Jiang Z, Guo T, Ding Y. Effect of remineralizing agents on white spot lesions after orthodontic treatment: a systematic review. Am J Orthod Dentofacial Orthop. 2013 Mar;143(3):376-382.e3. doi: 10.1016/j.ajodo.2012.10.013. | not an orthodontic intervention |
| 99. AJODO | 2013 | Fleming PS, Eliades T, Katsaros C, Pandis N. Curing lights for orthodontic bonding: a systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2013 Apr;143(4 Suppl):S92-103. doi: 10.1016/j.ajodo.2012.07.018. | not an orthodontic intervention |
| 100.AJODO | 2013 | Kloukos D, Pandis N, Eliades T. Bisphenol-A and residual monomer leaching from orthodontic adhesive resins and polycarbonate brackets: a systematic review. Am J Orthod Dentofacial Orthop. 2013 Apr;143(4 Suppl):S104-12.e1-2. doi: 10.1016/j.ajodo.2012.11.015. | not an orthodontic intervention |
| 101.AJODO | 2013 | Hua F, He H, Ngan P, Bouzid W. Prevalence of peg-shaped maxillary permanent lateral incisors: A meta-analysis. Am J Orthod Dentofacial Orthop. 2013 Jul;144(1):97-109. doi: 10.1016/j.ajodo.2013.02.025. | not an orthodontic intervention |
| 102.AJODO | 2012 | Fleming PS, Johal A, Pandis N. Self-etch primers and conventional acid-etch technique for orthodontic bonding: a systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2012 Jul;142(1):83-94. doi: 10.1016/j.ajodo.2012.02.023. | not an orthodontic intervention |
| 103.AJODO | 2012 | Hafez HS, Shaarawy SM, Al-Sakiti AA, Mostafa YA. Dental crowding as a caries risk factor: a systematic review. Am J Orthod Dentofacial Orthop. 2012 Oct;142(4):443-50. doi: 10.1016/j.ajodo.2012.04.018. | not an orthodontic intervention |
| 104.AJODO | 2012 | Meursinge Reynders RA, Ronchi L, Ladu L, van Etten-Jamaludin F, Bipat S. Insertion torque and success of orthodontic mini-implants: a systematic review. Am J Orthod Dentofacial Orthop. 2012 Nov;142(5):596-614.e5. doi: 10.1016/j.ajodo.2012.06.013. | not the effects of orthodontic interventions were assessed |
| 105.AJODO | 2012 | Papageorgiou SN, Zogakis IP, Papadopoulos MA. Failure rates and associated risk factors of orthodontic miniscrew implants: a meta-analysis. Am J Orthod Dentofacial Orthop. 2012 Nov;142(5):577-595.e7. doi: 10.1016/j.ajodo.2012.05.016. | not the effects of orthodontic interventions were assessed |
| 106.AJODO | 2010 | Crismani AG, Bertl MH, Celar AG, Bantleon HP, Burstone CJ. Miniscrews in orthodontic treatment: review and analysis of published clinical trials. Am J Orthod Dentofacial Orthop. 2010 Jan;137(1):108-13. doi: 10.1016/j.ajodo.2008.01.027. | not the effects of orthodontic interventions were assessed |

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| 107.AJODO | 2010 | Weltman B, Vig KW, Fields HW, Shanker S, Kaizar EE. Root resorption associated with orthodontic tooth movement: a systematic review. Am J Orthod Dentofacial Orthop. 2010 Apr;137(4):462-76; discussion 12A. doi: 10.1016/j.ajodo.2009.06.021. | assessed exclusively adverse effects |
| 108.AJODO | 2010 | Finnema KJ, Ozcan M, Post WJ, Ren Y, Dijkstra PU. In-vitro orthodontic bond strength testing: a systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2010 May;137(5):615-622.e3. doi: 10.1016/j.ajodo.2009.12.021. | review of laboratory studies |
| 109.AJODO | 2010 | Rogers S, Chadwick B, Treasure E. Fluoride-containing orthodontic adhesives and decalcification in patients with fixed appliances: a systematic review. Am J Orthod Dentofacial Orthop. 2010 Oct;138(4):390.e1-8; discussion 390-1. doi: 10.1016/j.ajodo.2010.02.025. | not an orthodontic intervention |
| 110.AJODO | 2010 | Ahrens A, McGrath C, Hägg U. Subjective efficacy of oral appliance design features in the management of obstructive sleep apnea: a systematic review. Am J Orthod Dentofacial Orthop. 2010 Nov;138(5):559-76. doi: 10.1016/j.ajodo.2010.01.030. | not an orthodontic intervention |
| 111.AJODO | 2009 | Al-Riyami S, Moles DR, Cunningham SJ. Orthognathic treatment and temporomandibular disorders: a systematic review. Part 1. A new quality-assessment technique and analysis of study characteristics and classifications. Am J Orthod Dentofacial Orthop. 2009 Nov;136(5):624.e1-15; discussion 624-5. doi: 10.1016/j.ajodo.2009.02.021. | not the effects of orthodontic interventions were assessed |
| 112.AJODO | 2009 | Al-Riyami S, Cunningham SJ, Moles DR. Orthognathic treatment and temporomandibular disorders: a systematic review. Part 2. Signs and symptoms and meta-analyses. Am J Orthod Dentofacial Orthop. 2009 Nov;136(5):626.e1-16, discussion 626-7. doi: 10.1016/j.ajodo.2009.02.022. | not the effects of orthodontic interventions were assessed |
| 113.AO | 2021 | Santana LG, Avelar K, Marques LS. Association between arch perimeter management and the occurrence of mandibular second molar eruption disturbances. Angle Orthod. 2021 Jul 1;91(4):544-554. doi: 10.2319/091720-799.1. PMID: 33587114; PMCID: PMC8259765. | not the effects of orthodontic interventions were assessed |
| 114.AO | 2021 | Li Z, Zhou J, Chen S. The effectiveness of locally injected platelet-rich plasma on orthodontic tooth movement acceleration. Angle Orthod. 2021 May 1;91(3):391-398. doi: 10.2319/061320-544.1. PMID: 33566068; PMCID: PMC8084470. | review of animal studies |
| 115.AO | 2021 | Veginadu P, Tavva SR, Muddada V, Gorantla S. Effect of pharmacological agents on relapse following orthodontic tooth movement. Angle Orthod. 2020 Jul 1;90(4):598-606. doi: 10.2319/092619-613.1. PMID: 33378496; PMCID: PMC8028453. | review of animal studies |
| 116.AO | 2020 | Yao K, Zhu G, Chen M, Zhang B, Wu Y, Li P. Effect of surgery-first orthognathic approach on oral health-related quality of life. Angle Orthod. 2020 Sep 1;90(5):723-733. doi: 10.2319/112619-749.1. | review included orthognathic surgical interventions |

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| | | Erratum in: Angle Orthod. 2021 Mar 1;91(2):279-281. PMID: 33378482; PMCID: PMC8032263. | |
| 117.AO | 2019 | Sam A, Currie K, Oh H, Flores-Mir C, Lagravére-Vich M. Reliability of different three-dimensional cephalometric landmarks in cone-beam computed tomography: A systematic review. Angle Orthod. 2019 Mar;89(2):317-332. doi: 10.2319/042018-302.1. Epub 2018 Nov 13. | not an orthodontic intervention |
| 118.AO | 2019 | Bastos RTDRM, Blagitz MN, Aragón MLSC, Maia LC, Normando D.Periodontal side effects of rapid and slow maxillary expansion: A systematic review. Angle Orthod. 2019 Jul;89(4):651-660. doi: 10.2319/060218-419.1. Epub 2019 Feb 11. | assessed exclusively adverse effects |
| 119.AO | 2018 | Ponce-Garcia C, Lagravere-Vich M, Cevidanes LHS, de Olivera Ruellas AC, Carey J, Flores-Mir C. Reliability of three-dimensional anterior cranial base superimposition methods for assessment of overall hard tissue changes: A systematic review. Angle Orthod. 2018 Mar;88(2):233-245. doi: 10.2319/071217-468.1. | not an orthodontic intervention |
| 120.AO | 2018 | Lima IFP, de Andrade Vieira W, de Macedo Bernardino Í, Costa PA, Lima APB, Pithon MM, Paranhos LR. Influence of reminder therapy for controlling bacterial plaque in patients undergoing orthodontic treatment: A systematic review and meta-analysis. Angle Orthod. 2018 Jul;88(4):483-493. doi: 10.2319/111117-770.1. | not an orthodontic intervention |
| 121.AO | 2018 | Sun W, Xia K, Tang L, Liu C, Zou L, Liu J. Accuracy of panoramic radiography in diagnosing maxillary sinus-root relationship: A systematic review and meta-analysis.Angle Orthod. 2018 Nov;88(6):819-829. doi: 10.2319/022018-135.1. | not an orthodontic intervention |
| 122.AO | 2017 | Eslami E, Katz ES, Baghdady M, Abramovitch K, Masoud MI. Are three-dimensional airway evaluations obtained through computed and cone-beam computed tomography scans predictable from lateral cephalograms? A systematic review of evidence. Angle Orthod. 2017 Jan;87(1):159-167. doi: 10.2319/032516-243.1. | not an orthodontic intervention |
| 123.AO | 2017 | Yi J, Sun Y, Li Y, Li C, Li X, Zhao Z. Cone-beam computed tomography versus periapical radiograph for diagnosing external root resorption: A systematic review and meta-analysis. Angle Orthod. 2017 Mar;87(2):328-337. doi: 10.2319/061916-481.1. | not an orthodontic intervention |
| 124.AO | 2017 | Currie K, Sawchuk D, Saltaji H, Oh H, Flores-Mir C, Lagravere M. Posterior cranial base natural growth and development: A systematic review. Angle Orthod. 2017 Nov;87(6):897-910. doi: 10.2319/032717-218.1. | not an orthodontic intervention |
| 125.AO | 2016 | Pachêco-Pereira C, Abreu LG, Dick BD, De Luca Canto G, Paiva SM, Flores-Mir C. Patient satisfaction after orthodontic treatment combined with orthognathic surgery: A systematic review. Angle Orthod. 2016 May;86(3):495-508. doi: 10.2319/040615-227.1. | review included orthognathic surgical interventions |

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| 126.AO | 2016 | Gong A, Li J, Wang Z, Li Y, Hu F, Li Q, Miao D, Wang L. Cranial base characteristics in anteroposterior malocclusions: A meta-analysis.Angle Orthod. 2016 Jul;86(4):668-80. doi: 10.2319/032315-186.1. | not an orthodontic intervention |
| 127.AO | 2016 | Maniewicz Wins S, Antonarakis GS, Kiliaridis S. Predictive factors of sagittal stability after treatment of Class II malocclusions. Angle Orthod. 2016 Nov;86(6):1033-1041. | not the effects of orthodontic interventions were assessed |
| 128.AO | 2016 | Aminoshariae A, Aminoshariae A, Valiathan M, Kulild JC. Association of genetic polymorphism and external apical root resorption. Angle Orthod. 2016 Nov;86(6):1042-1049. | assessed exclusively adverse effects |
| 129.AO | 2016 | Rossini G, Parrini S, Castroflorio T, Fortini A, Deregibus A, Debernardi CL. Children's perceptions of smile esthetics and their influence on social judgment. Angle Orthod. 2016 Nov;86(6):1050-1055. | not an orthodontic intervention |
| 130.AO | 2015 | Aljabaa A, McDonald F, Newton JT. A systematic review of randomized controlled trials of interventions to improve adherence among orthodontic patients aged 12 to 18. Angle Orthod. 2015 Mar;85(2):305-13. doi: 10.2319/031214-184.1. | not an orthodontic intervention |
| 131.AO | 2015 | Pachêco-Pereira C, De Luca Canto G, Major PW, Flores-Mir C. Variation of orthodontic treatment decision-making based on dental model type: A systematic review. Angle Orthod. 2015 May;85(3):501-9. doi: 10.2319/051214-343.1. | not the effects of orthodontic interventions were assessed |
| 132.AO | 2015 | Al-Jewair TS. Meta-analysis on the mandibular dimensions effects of the MARA appliance in patients with Class II malocclusions. Angle Orthod. 2015 Jul;85(4):706-14. doi: 10.2319/052814-378.1. | only one reviewer |
| 133.AO | 2014 | Grewal Bach GK, Torrealba Y, Lagravère MO. Orthodontic bonding to porcelain: a systematic review. Angle Orthod. 2014 May;84(3):555-60. doi: 10.2319/083013-636.1. | not the effects of orthodontic interventions were assessed |
| 134.AO | 2014 | Marquezan M, Mattos CT, Sant'Anna EF, de Souza MM, Maia LC. Does cortical thickness influence the primary stability of miniscrews?: A systematic review and meta-analysis. Angle Orthod. 2014 Nov;84(6):1093-103. doi: 10.2319/093013-716.1. | not the effects of orthodontic interventions were assessed |
| 135.AO | 2013 | Lione R, Franchi L, Cozza P. Does rapid maxillary expansion induce adverse effects in growing subjects? Angle Orthod. 2013 Jan;83(1):172-82. doi: 10.2319/041012-300.1. | assessed exclusively adverse effects |
| 136.AO | 2012 | Al-Anezi SA, Harradine NW. Quantifying plaque during orthodontic treatment:. Angle Orthod. 2012 Jul;82(4):748-53. doi: 10.2319/050111-312.1. | assessed exclusively adverse effects |
| 137.AO | 2012 | Luu NS, Nikolcheva LG, Retrouvey JM, Flores-Mir C, El-Bialy T, Carey JP, Major PW. Linear measurements using virtual study models. Angle Orthod. 2012 Nov;82(6):1098-106. doi: 10.2319/110311-681.1. | not an orthodontic intervention |
| 138.AO | 2012 | Saltaji H, Major MP, Altalibi M, Youssef M, Flores-Mir C. Long-term skeletal stability after maxillary advancement with distraction osteogenesis in cleft | assessed exclusively patients with |

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| | | lip and palate patients. Angle Orthod. 2012 Nov;82(6):1115-22. doi: 10.2319/011212-27.1. | congenital anomalies |
| 139.AO | 2012 | Santiago RC, de Miranda Costa LF, Vitral RW, Fraga MR, Bolognese AM, Maia LC. Cervical vertebral maturation as a biologic indicator of skeletal maturity. Angle Orthod. 2012 Nov;82(6):1123-31. doi: 10.2319/103111-673.1. | not an orthodontic intervention |
| 140.AO | 2010 | Archambault A, Lacoursiere R, Badawi H, Major PW, Carey J, Flores-Mir C. Torque expression in stainless steel orthodontic brackets. A systematic review. Angle Orthod. 2010 Jan;80(1):201-10. doi: 10.2319/080508-352.1. | review of laboratory studies |
| 141.AO | 2010 | Xiaoting L, Yin T, Yangxi C. Interventions for pain during fixed orthodontic appliance therapy. A systematic review. Angle Orthod. 2010 Sep;80(5):925-32. doi: 10.2319/010410-10.1. | not the effects of orthodontic interventions were assessed |
| 142.AO | 2010 | Magalhães IB, Pereira LJ, Marques LS, Gameiro GH. The influence of malocclusion on masticatory performance. A systematic review. Angle Orthod. 2010 Sep;80(5):981-7. doi: 10.2319/011910-33.1. | not the effects of orthodontic interventions were assessed |
| 143.KJO | 2021 | Giudice AL, Rustico L, Longo M, Oteri G, Papadopoulos MA, Nucera R. Complications reported with the use of orthodontic miniscrews: A systematic review. Korean J Orthod. 2021 May 25;51(3):199-216. doi: 10.4041/kjod.2021.51.3.199. PMID: 33984227; PMCID: PMC8133901. | assessed exclusively adverse effects |
| 144.KJO | 2021 | Sivarajan S, Mani SA, John J, Fayed MMS, Kook YA, Wey MC. The global distribution of permanent canine hypodontia: A systematic review. Korean J Orthod. 2021 Jan 25;51(1):55-74. doi: 10.4041/kjod.2021.51.1.55. PMID: 33446621; PMCID: PMC7837799. | not the effects of orthodontic interventions were assessed |
| 145.KJO | 2018 | Savoldi F, Papoutsi A, Dianiskova S, Dalessandri D, Bonetti S, Tsoi JKH, Matinlinna JP, Paganelli C. Resistance to sliding in orthodontics: misconception or method error? A systematic review and a proposal of a test protocol.Korean J Orthod. 2018 Jul;48(4):268-280. doi: 10.4041/kjod.2018.48.4.268. | review of laboratory studies |
| 146.KJO | 2018 | Nowrin SA, Jaafar S, Ab Rahman N, Basri R, Alam MK, Shahid F. Association between genetic polymorphisms and external apical root resorption: A systematic review and meta-analysis.Korean J Orthod. 2018 Nov;48(6):395-404. doi: 10.4041/kjod.2018.48.6.395. | assessed exclusively adverse effects |
| 147.KJO | 2016 | Hong SB, Kusnoto B, Kim EJ, BeGole EA, Hwang HS, Lim HJ. Prognostic factors associated with the success rates of posterior orthodontic miniscrew implants: A subgroup meta-analysis. Korean J Orthod. 2016 Mar;46(2):111-26. doi: 10.4041/kjod.2016.46.2.111. | not the effects of orthodontic interventions were assessed |
| 148.KJO | 2016 | Sawchuk D, Currie K1 Vich ML, Palomo JM, Flores-Mir C. Diagnostic methods for assessing maxillary skeletal and dental transverse deficiencies: A systematic review. Korean J Orthod. 2016 Sep;46(5):331-42. doi: 10.4041/kjod.2016.46.5.331. | not the effects of orthodontic interventions were assessed |

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| 149.KJO | 2015 | Alessandri-Bonetti G, Ippolito DR, Bartolucci ML, D'Antò V, Incerti-Parenti S. Cephalometric predictors of treatment outcome with mandibular advancement devices in adult patients with obstructive sleep apnea: a systematic review. Korean J Orthod. 2015 Nov;45(6):308-21. doi: 10.4041/kjod.2015.45.6.308. | not the effects of orthodontic interventions were assessed |
| 150.O&C | 2021 | Berry S, Javed F, Rossouw PE, Barmak AB, Kalogirou EM, Michelogiannakis D. Influence of thyroxine supplementation on orthodontically induced tooth movement and/or inflammatory root resorption: A systematic review. Orthod Craniofac Res. 2021 May;24(2):206-213. doi: 10.1111/ocr.12428. Epub 2020 Oct 18. PMID: 32991769. | review of animal studies |
| 151.O&C | 2021 | Roomaney IA, Chetty M. Sella turcica morphology in patients with genetic syndromes: A systematic review. Orthod Craniofac Res. 2021 May;24(2):194-205. doi: 10.1111/ocr.12426. Epub 2020 Sep 28. PMID: 32920986. | not the effects of orthodontcis were assessed |
| 152.O&C | 2021 | Ahn HW, Kim SJ, Baek SH. Miniplate-anchored maxillary protraction in adolescent patients with cleft lip and palate: A literature review of study design, type and protocol, and treatment outcomes. Orthod Craniofac Res. 2021 Mar;24 Suppl 1:21-30. doi: 10.1111/ocr.12446. Epub 2020 Dec 7. PMID: 33253469. | assessed exclusively patients with congenital anomalies |
| 153.O&C | 2021 | Kaklamanos EG, Makrygiannakis MA, Athanasiou AE. Could medications and biologic factors affect post-orthodontic tooth movement changes? A systematic review of animal studies. Orthod Craniofac Res. 2021 Feb;24(1):39-51. doi: 10.1111/ocr.12411. Epub 2020 Aug 5. PMID: 32654394. | review of animal studies |
| 154.O&C | 2021 | Marques FBC, de Lima LS, Oliveira PLE, Magno MB, Ferreira DMTP, de Castro ACR, Maciel JVB, Ruellas ACO, Maia LC. Are temporomandibular disorders associated with facial asymmetry? A systematic review and meta-analysis. Orthod Craniofac Res. 2021 Feb;24(1):1-16. doi: 10.1111/ocr.12404. Epub 2020 Jul 19. PMID: 32608091. | not the effects of orthodontcis were assessed |
| 155.O&C | 2020 | Pinheiro FHSL, Drummond RJ, Frota CM, Bartzela TN, Dos Santos PB. Comparison of early and conventional autogenous secondary alveolar bone graft in children with cleft lip and palate: A systematic review. Orthod Craniofac Res. 2020 Nov;23(4):385-397. doi: 10.1111/ocr.12394. Epub 2020 Jun 28. PMID: 32446283. | assessed exclusively patients with congenital anomalies |
| 156.O&C | 2020 | Xiao WL, Jia KN, Yu G, Zhao N. Association between forkhead box E1 polymorphisms and risk of non-syndromic cleft lip with or without cleft palate: A meta-analysis. Orthod Craniofac Res. 2020 May;23(2):151-159. doi: 10.1111/ocr.12366. Epub 2020 Feb 5. PMID: 31944555. | not the effects of orthodontics were assessed |
| 157.O&C | 2020 | Kaklamanos EG, Makrygiannakis MA, Athanasiou AE. Do analgesics used for the pain experienced after orthodontic procedures affect tooth | review of animal studies |

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| | | movement rate? A systematic review based on animal studies. Orthod Craniofac Res. 2020 May;23(2):143-150. doi: 10.1111/ocr.12357. Epub 2019 Nov 9. PMID: 31705727. | |
| 158.O&C | 2020 | Elsten EECM, Caron CJJM, Dunaway DJ, Padwa BL, Forrest C, Koudstaal MJ. Dental anomalies in craniofacial microsomia: A systematic review. Orthod Craniofac Res. 2020 Feb;23(1):16-26. doi: 10.1111/ocr.12351. Epub 2019 Oct 28. PMID: 31608577; PMCID: PMC7003932. | not the effects of orthodontics were assessed |
| 159.O&C | 2020 | Wu Z, Zhang X, Li Z, Liu Y, Jin H, Chen Q, Guo J. A Bayesian network meta-analysis of orthopaedic treatment in Class III malocclusion: Maxillary protraction with skeletal anchorage or a rapid maxillary expander. Orthod Craniofac Res. 2020 Feb;23(1):1-15. doi: 10.1111/ocr.12339. Epub 2019 Sep 15. PMID: 31452316. | Bayesian network analysis was used |
| 160.O&C | 2019 | Fang X, Qi R, Liu C. Root resorption in orthodontic treatment with clear aligners: A systematic review and meta-analysis. Orthod Craniofac Res. 2019 Nov;22(4):259-269. doi: 10.1111/ocr.12337. Epub 2019 Aug 29. PMID: 31323701. | assessed exclusively adverse effects |
| 161.O&C | 2019 | Iliadi A, Koletsi D, Eliades T. Forces and moments generated by aligner-type appliances for orthodontic tooth movement: A systematic review and meta-analysis. Orthod Craniofac Res. 2019 Nov;22(4):248-258. doi: 10.1111/ocr.12333. Epub 2019 Jul 9. PMID: 31237410. | review of laboratory studies |
| 162.O&C | 2019 | Tarallo F, Chimenti C, Paiella G, Cordaro M, Tepedino M. Biomarkers in the gingival crevicular fluid used to detect root resorption in patients undergoing orthodontic treatment: A systematic review. Orthod Craniofac Res. 2019 Nov;22(4):236-247. doi: 10.1111/ocr.12329. Epub 2019 Jul 2. PMID: 31207100. | not the effects of orthodontic interventions were assessed |
| 163.O&C | 2019 | Tasios T, Papageorgiou SN, Papadopoulos MA, Tsapas A, Haidich AB. Prevention of orthodontic enamel demineralization: A systematic review with meta-analyses. Orthod Craniofac Res. 2019 Nov;22(4):225-235. doi: 10.1111/ocr.12322. Epub 2019 May 27. PMID: 31081584. | not the effects of orthodontic interventions were assessed |
| 164.O&C | 2018 | Javed F, Akram Z, Barillas AP, Kellesarian SV, Ahmed HB, Khan J, Almas K. Outcome of orthodontic palatal plate therapy for orofacial dysfunction in children with Down syndrome: A systematic review.Orthod Craniofac Res. 2018 Feb;21(1):20-26. doi: 10.1111/ocr.12211. | assessed exclusively patients with congenital anomalies |
| 165.O&C | 2018 | Papageorgiou SN, Xavier GM, Cobourne MT, Eliades T. Effect of orthodontic treatment on the subgingival microbiota: A systematic review and meta-analysis.Orthod Craniofac Res. 2018 Nov;21(4):175-185. doi: 10.1111/ocr.12237. | assessed exclusively adverse effects |
| 166.O&C | 2018 | Scariot R, Corso PFCL, Sebastiani AM, Vieira AR.The many faces of genetic contributions to temporomandibular joint disorder: An updated | not an orthodontic intervention |

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| | | review. Orthod Craniofac Res. 2018 Nov;21(4):186-201. doi: 10.1111/ocr.12239. Epub 2018 Sep 11. | |
| 167.O&C | 2017 | Antonarakis GS, Palaska PK2 Suri S. Permanent tooth agenesis in individuals with non-syndromic Robin sequence: a systematic review and meta-analysis. Orthod Craniofac Res. 2017 Nov;20(4):216-226. doi: 10.1111/ocr.12204. | assessed exclusively patients with congenital anomalies |
| 168.O&C | 2016 | Altmann AS, Collares FM, Leitune VC, Samuel SM. The effect of antimicrobial agents on bond strength of orthodontic adhesives: a meta-analysis of in vitro studies. Orthod Craniofac Res. 2016 Feb;19(1):1-9. doi: 10.1111/ocr.12100. Epub 2015 Aug 10. | review of laboratory studies |
| 169.O&C | 2015 | Tee BC, Sun Z. Mandibular distraction osteogenesis assisted by cell-based tissue engineering: a systematic review. Orthod Craniofac Res. 2015 Apr;18 Suppl 1:39-49. doi: 10.1111/ocr.12087. (in suppl issue) | review included orthognathic surgical interventions |
| 170.O&C | 2015 | De Luca Canto G, Pachêco-Pereira C, Lagravere MO, Flores-Mir C, Major PW. Intra-arch dimensional measurement validity of laser-scanned digital dental models compared with the original plaster models: a systematic review. Orthod Craniofac Res. 2015 May;18(2):65-76. doi: 10.1111/ocr.12068. | not an orthodontic intervention |
| 171.O&C | 2015 | Austin SL, Mattick CR, Waterhouse PJ. Distraction osteogenesis versus orthognathic surgery for the treatment of maxillary hypoplasia in cleft lip and palate patients: a systematic review. Orthod Craniofac Res. 2015 May;18(2):96-108. doi: 10.1111/ocr.12063. | review included orthognathic surgical interventions |
| 172.O&C | 2014 | Koretsi V, Chatzigianni A, Sidiropoulou S. Enamel roughness and incidence of caries after interproximal enamel reduction: a systematic review. Orthod Craniofac Res. 2014 Feb;17(1):1-13. doi: 10.1111/ocr.12030. | not an orthodontic intervention |
| 173.O&C | 2014 | Pittayapat P, Limchaichana-Bolstad N, Willems G, Jacobs R. Three-dimensional cephalometric analysis in orthodontics: a systematic review. Orthod Craniofac Res. 2014 May;17(2):69-91. doi: 10.1111/ocr.12034. | not an orthodontic intervention |
| 174.O&C | 2013 | Perinetti G, Primožič J, Castaldo A, Di Lenarda R, Contardo L. Is gingival crevicular fluid volume sensitive to orthodontic tooth movement? A systematic review of split-mouth longitudinal studies. Orthod Craniofac Res. 2013 Feb;16(1):1-19. doi: 10.1111/ocr.12005. | assessed exclusively adverse effects |
| 175.O&C | 2013 | Andrade DC, Loureiro CA, Araújo VE, Riera R, Atallah AN. Treatment for agenesis of maxillary lateral incisors: a systematic review. Orthod Craniofac Res. 2013 Aug;16(3):129-36. doi: 10.1111/ocr.12015. | empty review |
| 176.O&C | 2012 | Angelopoulou MV, Vlachou V, Halazonetis DJ. Pharmacological management of pain during orthodontic treatment: a meta-analysis. Orthod Craniofac Res. 2012 May;15(2):71-83. doi: 10.1111/j.1601-6343.2012.01542.x. | assessed exclusively adverse effects |

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| 177.O&C | 2012 | Gritsch K, Laroche N, Morgon L, Al-Hity R, Vico L, Colon P, Grosgogeat B. A systematic review of methods for tissue analysis in animal studies on orthodontic mini-implants. Orthod Craniofac Res. 2012 Aug;15(3):135-47. doi: 10.1111/j.1601-6343.2012.01548.x. | review of animal studies |
| 178.O&C | 2012 | Papadopoulos MA, Koumpridou EN, Vakalis ML, Papageorgiou SN. Effectiveness of pre-surgical infant orthopedic treatment for cleft lip and palate patients: a systematic review and meta-analysis. Orthod Craniofac Res. 2012 Nov;15(4):207-36. doi: 10.1111/j.1601-6343.2012.01552.x. | assessed exclusively patients with congenital anomalies |
| 179.O&C | 2011 | Fleming PS, Marinho V, Johal A. Orthodontic measurements on digital study models compared with plaster models: a systematic review. Orthod Craniofac Res. 2011 Feb;14(1):1-16. doi: 10.1111/j.1601-6343.2010.01503.x. | not an orthodontic intervention |
| 180.O&C | 2010 | Joss-Vassalli I, Grebenstein C, Topouzelis N, Sculean A, Katsaros C. Orthodontic therapy and gingival recession: a systematic review. Orthod Craniofac Res. 2010 Aug;13(3):127-41. doi: 10.1111/j.1601-6343.2010.01491.x. | assessed exclusively adverse effects |

*Description of the abbreviated journals:
Cochrane library: Cochrane Database of Systematic Reviews
AJODO: American Journal of Orthodontics and Dentofacial Orthopedics
EJO: European Journal of Orthodontics
AO: Angle Orthodontist
KJO: Korean Journal of Orthodontics
O&CR: Orthodontics and Craniofacial Research

**Excluded studies during the full text screening (n=45) with the rationale for exclusion**

| Journal* | Year | Reference | Rationale for exclusion |
|---|---|---|---|
| 1. Cochrane library | 2017 | Parkin N, Benson PE, Thind B, Shah A, Khalil I, Ghafoor S. Open versus closed surgical exposure of canine teeth that are displaced in the roof of the mouth.Cochrane Database Syst Rev. 2017 Aug 21;8:CD006966. doi: 10.1002/14651858.CD006966.pub3. | not the effects of orthodontic interventions were assessed |
| 2. Cochrane library | 2016 | Littlewood SJ, Millett DT, Doubleday B, Bearn DR, Worthington HV. Retention procedures for stabilising tooth position after treatment with orthodontic braces. Cochrane Database Syst Rev. 2016 Jan 29;(1):CD002283. doi: 10.1002/14651858.CD002283.pub4. | assessed exclusively adverse effects |
| 3. EJO | 2020 | Rekhi U, Catunda RQ, Gibson MP. Surgically accelerated orthodontic techniques and periodontal response: a systematic review. Eur J Orthod. 2020 Jan 15:cjz103. doi: 10.1093/ejo/cjz103. Epub ahead of print. PMID: 31942984. | the review is about a specific outcome of an intervention, which is ambiguous and could also be an adverse effect |
| 4. EJO | 2020 | Bortolotti F, Solidoro L, Bartolucci ML, Incerti Parenti S, Paganelli C, Alessandri-Bonetti G. Skeletal and dental effects of surgically assisted rapid palatal expansion: a systematic review of randomized controlled trials. Eur J Orthod. 2020 Sep 11;42(4):434-440. doi: 10.1093/ejo/cjz057. PMID: 31365925. | review included orthognathic surgical interventions |
| 5. EJO | 2020 | Papageorgiou SN, Koletsi D, Iliadi A, Peltomaki T, Eliades T. Treatment outcome with orthodontic aligners and fixed appliances: a systematic review with meta-analyses. Eur J Orthod. 2020 Jun 23;42(3):331-343. doi: 10.1093/ejo/cjz094. PMID: 31758191. | review included orthognathic surgical interventions |
| 6. EJO | 2019 | Bellini-Pereira SA, Pupulim DC, Aliaga-Del Castillo A, Henriques JFC, Janson G. Time of maxillary molar distalization with non-compliance intraoral distalizing appliances: a meta-analysis. Eur J Orthod. 2019 Nov 15;41(6):652-660. doi: 10.1093/ejo/cjz030. PMID: 31107942. | the review is about a specific outcome of an intervention, which is ambiguous and could also be an adverse effect |
| 7. EJO | 2019 | Swidi AJ, Griffin AE, Buschang PH. Mandibular alignment changes after full-fixed orthodontic treatment: a systematic review and meta-analysis. Eur J Orthod. 2019 Nov 15;41(6):609-621. Doi: 10.1093/ejo/cjz004. PMID: 30788505. | assessed exclusively adverse effects |
| 8. EJO | 2019 | Phuong A, Fagundes NCF, Abtahi S, Roberts MR, Major PW, Flores-Mir C. Additional appointments and discomfort associated with compliance-free | assessed exclusively adverse effects |

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| | | fixed Class II corrector treatment: a systematic review. Eur J Orthod. 2019 Aug 8;41(4):404-414. Doi: 10.1093/ejo/cjy074. | |
| 9. EJO | 2019 | Almuzian M, Rizk MZ, Ulhaq A, Alharbi F, Alomari S, Mohammed H. Effectiveness of different debonding techniques and adjunctive methods on pain and discomfort perception during debonding fixed orthodontic appliances: a systematic review. Eur J Orthod. 2019 Sep 21;41(5):486-494. doi: 10.1093/ejo/cjz013. PMID: 30934051. | not an orthodontic intervention review |
| 10. EJO | 2018 | Cassina C, Papageorgiou SN, Eliades T. Open versus closed surgical exposure for permanent impacted canines: a systematic review and meta-analyses.Eur J Orthod. 2018 Jan 23;40(1):1-10. doi: 10.1093/ejo/cjx047. | not the effects of orthodontic interventions were assessed |
| 11. EJO | 2018 | Sampaziotis D, Tsolakis IA, Bitsanis E, Tsolakis AI. Open versus closed surgical exposure of palatally impacted maxillary canines: comparison of the different treatment outcomes-a systematic review.Eur J Orthod. 2018 Jan 23;40(1):11-22. doi: 10.1093/ejo/cjw077. | not the effects of orthodontic interventions were assessed |
| 12. EJO | 2018 | Papageorgiou SN, Papadelli AA, Eliades T. Effect of orthodontic treatment on periodontal clinical attachment: a systematic review and meta-analysis.Eur J Orthod. 2018 Apr 6;40(2):176-194. doi: 10.1093/ejo/cjx052. | assessed exclusively adverse effects |
| 13. EJO | 2017 | Buzatta LN, Shimizu RH, Shimizu IA, Pachêco-Pereira C, Flores-Mir C, Taba M Jr, Porporatti AL, De Luca Canto G. Gingival condition associated with two types of orthodontic fixed retainers: a meta-analysis. Eur J Orthod. 2017 Aug 1;39(4):446-452. doi: 10.1093/ejo/cjw057. | assessed exclusively adverse effects |
| 14. EJO | 2017 | Buck LM, Dalci O, Darendeliler MA, Papageorgiou SN, Papadopoulou AK. Volumetric upper airway changes after rapid maxillary expansion: a systematic review and meta-analysis. Eur J Orthod. 2017 Oct 1;39(5):463-473. doi: 10.1093/ejo/cjw048. | review included orthognathic surgical interventions |
| 15. EJO | 2016 | Bock NC, von Bremen J, Ruf S. Stability of Class II fixed functional appliance therapy--a systematic review and meta-analysis. Eur J Orthod. 2016 Apr;38(2):129-39. doi: 10.1093/ejo/cjv009. | assessed exclusively adverse effects |
| 16. EJO | 2016 | Sollenius O, Petrén S, Björnsson L, Norlund A, Bondemark L. Health economic evaluations in orthodontics: a systematic review. Eur J Orthod. 2016 Jun;38(3):259-65. doi: 10.1093/ejo/cjv040. | review did not assess the effect of a specific type of intervention(s), but assessed an undefined orthodontic intervention, e.g., orthodontic treatment as a whole |
| 17. EJO | 2016 | Janson G, Mendes LM, Junqueira CH, Garib DG. Soft-tissue changes in Class II malocclusion patients | review included orthognathic |

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| | | treated with extractions: a systematic review. Eur J Orthod. 2016 Dec;38(6):631-637. | surgical interventions |
| 18. EJO | 2015 | Rossini G, Parrini S, Castroflorio T, Deregibus A, Debernardi CL. Periodontal health during clear aligners treatment: a systematic review. Eur J Orthod. 2015 Oct;37(5):539-43. doi: 10.1093/ejo/cju083. | assessed exclusively adverse effects |
| 19. EJO | 2014 | Yepes E, Quintero P, Rueda ZV, Pedroza A. Optimal force for maxillary protraction facemask therapy in the early treatment of class III malocclusion. Eur J Orthod. 2014 Oct;36(5):586-94. doi: 10.1093/ejo/cjt091. | not the effects of orthodontic interventions were assessed |
| 20. AJODO | 2020 | Pacha MM, Fleming PS, Johal A. Complications, impacts, and success rates of different approaches to treatment of Class II malocclusion in adolescents: A systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2020 Oct;158(4):477-494.e7. doi: 10.1016/j.ajodo.2020.03.021. Epub 2020 Sep 2. PMID: 32888735. | assessed exclusively adverse effects |
| 21. AJODO | 2020 | Vandersluis YR, Suri S. Infective endocarditis and orthodontic implications in children: A review of the literature. Am J Orthod Dentofacial Orthop. 2020 Jan;157(1):19-28. doi: 10.1016/j.ajodo.2019.03.027. PMID: 31901273. | not the effects of orthodontic interventions were assessed |
| 22. AJODO | 2017 | Javidi H, Vettore M, Benson PE. Does orthodontic treatment before the age of 18 years improve oral health-related quality of life? A systematic review and meta-analysis. Am J Orthod Dentofacial Orthop. 2017 Apr;151(4):644-655. doi: 10.1016/j.ajodo.2016.12.011. | review did not assess the effect of a specific type of intervention(s), but assessed an undefined orthodontic intervention, e.g., orthodontic treatment as a whole |
| 23. AJODO | 2016 | Tsichlaki A, Chin SY, Pandis N, Fleming PS. How long does treatment with fixed orthodontic appliances last? A systematic review. Am J Orthod Dentofacial Orthop. 2016 Mar;149(3):308-18. doi: 10.1016/j.ajodo.2015.09.020. | review did not assess the effect of a specific type of intervention(s), but assessed an undefined orthodontic intervention, e.g., orthodontic treatment as a whole |
| 24. AJODO | 2015 | Pachêco-Pereira C, Pereira JR, Dick BD, Perez A, Flores-Mir C. Factors associated with patient and parent satisfaction after orthodontic treatment: a systematic review. Am J Orthod Dentofacial Orthop. 2015 Oct;148(4):652-9. doi: 10.1016/j.ajodo.2015.04.039. | review did not assess the effect of a specific type of intervention(s), but assessed an undefined orthodontic |

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| | | | intervention, e.g., orthodontic treatment as a whole |
| 25. AJODO | 2014 | Mai W, He J, Meng H, Jiang Y, Huang C, Li M, Yuan K, Kang N. Comparison of vacuum-formed and Hawley retainers: a systematic review. Am J Orthod Dentofacial Orthop. 2014 Jun;145(6):720-7. doi: 10.1016/j.ajodo.2014.01.019. | assessed exclusively adverse effects |
| 26. AJODO | 2011 | Greenlee GM, Huang GJ, Chen SS, Chen J, Koepsell T, Hujoel P. Stability of treatment for anterior open-bite malocclusion: a meta-analysis. Am J Orthod Dentofacial Orthop. 2011 Feb;139(2):154-69. doi: 10.1016/j.ajodo.2010.10.019. | review included orthognathic surgical interventions |
| 27. AJODO | 2010 | Viglianisi A. Effects of lingual arch used as space maintainer on mandibular arch dimension: a systematic review. Am J Orthod Dentofacial Orthop. 2010 Oct;138(4):382.e1-4; discussion 382-3. doi: 10.1016/j.ajodo.2010.02.026. | review was conducted by one operator only |
| 28. AO | 2021 | Santana LG, Marques LS. Do adjunctive interventions in patients undergoing rapid maxillary expansion increase the treatment effectiveness? Angle Orthod. 2021 Jan 1;91(1):119-128. doi: 10.2319/051320-431.1. PMID: 33289794; PMCID: PMC8032281. | review included orthognathic surgical interventions |
| 29. AO | 2020 | Mecenas P, Espinosa DG, Cardoso PC, Normando D. Stainless steel or titanium mini-implants? Angle Orthod. 2020 Jul 1;90(4):587-597. doi: 10.2319/081619-536.1. PMID: 33378494; PMCID: PMC8028470. | not the effects of orthodontic interventions were assessed |
| 30. AO | 2020 | Moda LB, da Silva Barros ALC, Fagundes NCF, Normando D, Maia LC, Mendes SMDA. Lower fixed retainers: bonded on all teeth or only on canines? A systematic review. Angle Orthod. 2020 Jan;90(1):125-143. doi: 10.2319/013019-63.1. Epub 2019 Sep 19. PMID: 31536378; PMCID: PMC8087051. | assessed exclusively adverse effects |
| 31. AO | 2019 | Alakttash AM, Fawzi M, Bearn D. Adhesive precoated bracket systems and operator coated bracket systems: Is there any difference? A systematic review and meta-analysis. Angle Orthod. 2019 May;89(3):495-504. doi: 10.2319/051818-373.1. Epub 2018 Dec 17. | assessed exclusively adverse effects |
| 32. AO | 2017 | Diar-Bakirly S, Feres MF, Saltaji H, Flores-Mir C, El-Bialy T. Effectiveness of the transpalatal arch in controlling orthodontic anchorage in maxillary premolar extraction cases: A systematic review and meta-analysis.Angle Orthod. 2017 Jan;87(1):147-158. doi: 10.2319/021216-120.1. | assessed exclusively adverse effects |
| 33. AO | 2017 | Almasoud NN. Extraction of primary canines for interceptive orthodontic treatment of palatally displaced permanent canines: A systematic review. Angle Orthod. 2017 Nov;87(6):878-885. doi: 10.2319/021417-105.1. | not the effects of orthodontic interventions were assessed |
| 34. AO | 2015 | Andiappan M, Gao W, Bernabé E, Kandala NB, Donaldson AN. Malocclusion, orthodontic | review included orthognathic |

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| | | treatment, and the Oral Health Impact Profile (OHIP-14): Systematic review and meta-analysis. Angle Orthod. 2015 May;85(3):493-500. doi: 10.2319/051414-348.1. | surgical interventions |
| 35. AO | 2013 | Long H, Zhou Y, Pyakurel U, Liao L, Jian F, Xue J, Ye N, Yang X, Wang Y, Lai W. Comparison of adverse effects between lingual and labial orthodontic treatment. Angle Orthod. 2013 Nov;83(6):1066-73. doi: 10.2319/010113-2.1. | assessed exclusively adverse effects |
| 36. AO | 2011 | Janson G, Branco NC, Fernandes TM, Sathler R, Garib D, Lauris JR. Influence of orthodontic treatment, midline position, buccal corridor and smile arc on smile attractiveness. Angle Orthod. 2011 Jan;81(1):153-61. doi: 10.2319/040710-195.1. | review did not assess the effect of a specific type of intervention(s), but assessed an undefined orthodontic intervention, e.g., orthodontic treatment as a whole |
| 37. KJO | 2017 | Papageorgiou SN, Höchli D, Eliades T. Outcomes of comprehensive fixed appliance orthodontic treatment: A systematic review with meta-analysis and methodological overview. Korean J Orthod. 2017 Nov;47(6):401-413. doi: 10.4041/kjod.2017.47.6.401. | review did not assess the effect of a specific type of intervention(s), but assessed an undefined orthodontic intervention, e.g., orthodontic treatment as a whole |
| 38. O&CR | 2021 | Lee DW, Park JH, Bay RC, Choi SK, Chae JM. Cortical bone thickness and bone density effects on miniscrew success rates: A systematic review and meta-analysis. Orthod Craniofac Res. 2021 Mar;24 Suppl 1:92-102. doi: 10.1111/ocr.12453. Epub 2020 Dec 16. | not the effects of orthodontic interventions were assessed |
| 39. O&CR | 2021 | Lee DW, Park JH, Bay RC, Choi SK, Chae JM. Cortical bone thickness and bone density effects on miniscrew success rates: A systematic review and meta-analysis. Orthod Craniofac Res. 2021 Mar;24 Suppl 1:92-102. doi: 10.1111/ocr.12453. Epub 2020 Dec 16. | assessed exclusively adverse effects |
| 40. O&CR | 2021 | Lee DW, Park JH, Bay RC, Choi SK, Chae JM. Cortical bone thickness and bone density effects on miniscrew success rates: A systematic review and meta-analysis. Orthod Craniofac Res. 2021 Mar;24 Suppl 1:92-102. doi: 10.1111/ocr.12453. Epub 2020 Dec 16. | not the effects of orthodontic interventions were assessed |
| 41. O&CR | 2021 | Copello FM, Marañón-Vásquez GA, Brunetto DP, Caldas LD, Masterson D, Maia LC, Sant'Anna EF. Is the buccal alveolar bone less affected by mini-implant assisted rapid palatal expansion than by | assessed exclusively adverse effects |

| | | | |
|---|---|---|---|
| | | conventional rapid palatal expansion?-A systematic review and meta-analysis. Orthod Craniofac Res. 2020 Aug;23(3):237-249. doi: 10.1111/ocr.12374. Epub 2020 Apr 16. PMID: 32187843. | |
| 42. O&CR | 2019 | Allen RK, Edelmann AR, Abdulmajeed A, Bencharit S. Salivary protein biomarkers associated with orthodontic tooth movement: A systematic review. Orthod Craniofac Res. 2019 May;22 Suppl 1:14-20. doi: 10.1111/ocr.12258. | not the effects of orthodontic interventions were assessed |
| 43. O&CR | 2018 | Cannavale R, Chiodini P, Perillo L, Piancino MG. Rapid palatal expansion (RPE): Meta-analysis of long-term effects.Orthod Craniofac Res. 2018 Nov;21(4):225-235. doi: 10.1111/ocr.12244. | assessed exclusively adverse effects |
| 44. O&CR | 2015 | Al-Saleh MAQ, Alsufyani N, Flores-Mir C, Nebbe B, Major PW. Changes in temporomandibular joint morphology in class II patients treated with fixed mandibular repositioning and evaluated through 3D imaging: a systematic review. Orthod Craniofac Res. 2015 Nov;18(4):185-201. doi: 10.1111/ocr.12099. | the review is about a specific outcome of an intervention, which is ambiguous and could also be an adverse effect |
| 45. O&CR | 2011 | von Bremen J, Ruf S. Orthodontic and dentofacial orthopedic management of juvenile idiopathic arthritis: a systematic review of the literature. Orthod Craniofac Res. 2011 Aug;14(3):107-15. doi: 10.1111/j.1601-6343.2011.01514.x. | review included orthognathic surgical interventions |

*Description of the abbreviated journals:
Cochrane library: Cochrane Database of Systematic Reviews
AJODO: American Journal of Orthodontics and Dentofacial Orthopedics
EJO: European Journal of Orthodontics
AO: Angle Orthodontist
KJO: Korean Journal of Orthodontics
O&CR: Orthodontics and Craniofacial Research

## Additional files chapter 4

**Additional file 1. PRISMA-P Checklist**

### PRISMA-P 2015 Checklist

This checklist has been adapted for use with protocol submissions to *Systematic Reviews* from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1

| Section/topic | # | Checklist item | Information reported | | Line number(s) |
|---|---|---|---|---|---|
| | | | Yes | No | |
| **ADMINISTRATIVE INFORMATION** | | | | | |
| **Title** | | | | | |
| Identification | 1a | Identify the report as a protocol of a systematic review | x | ☐ | 2 |
| Update | 1b | If the protocol is for an update of a previous systematic review, identify as such | ☐ | x | Not an update |
| **Registration** | 2 | If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract | ☐ | x | Not a systematic review |
| **Authors** | | | | | |
| Contact | 3a | Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author | x | ☐ | 2 |
| Contributions | 3b | Describe contributions of protocol authors and identify the guarantor of the review | x | ☐ | 2 and 301-306 |
| **Amendments** | 4 | If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments | ☐ | x | Not an amendment |
| **Support** | | | | | |
| Sources | 5a | Indicate sources of financial or other support for the review | x | ☐ | 297-299 |
| Sponsor | 5b | Provide name for the review funder and/or sponsor | x | ☐ | 297-299 |
| Role of sponsor/funder | 5c | Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol | x | ☐ | 297-299 |
| **INTRODUCTION** | | | | | |
| **Rationale** | 6 | Describe the rationale for the review in the context of what is already known | x | ☐ | 61-109 |
| **Objectives** | 7 | Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) | x | ☐ | 110-117 |

| Section/topic | # | Checklist item | Information reported | | Line number(s) |
|---|---|---|---|---|---|
| | | | Yes | No | |
| **METHODS** | | | | | |
| **Eligibility criteria** | 8 | Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review | x | ☐ | 132-135 |
| **Information sources** | 9 | Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage | x | ☐ | 137-146 |
| **Search strategy** | 10 | Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated | x | ☐ | 138-141 |
| ***STUDY RECORDS*** | | | | | |
| Data management | 11a | Describe the mechanism(s) that will be used to manage records and data throughout the review | x | ☐ | 149-159 |
| Selection process | 11b | State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis) | x | ☐ | 160-170 |
| Data collection process | 11c | Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators | x | ☐ | 171-184 |
| **Data items** | 12 | List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications | x | ☐ | 186-205 |
| **Outcomes and prioritization** | 13 | List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale | x | ☐ | 186-223 |
| **Risk of bias in individual studies** | 14 | Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis | ☐ | x | Not applicable |
| ***DATA*** | | | | | |
| **Synthesis** | 15a | Describe criteria under which study data will be quantitatively synthesized | ☐ | x | Not a systematic review |
| | 15b | If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., $I^2$, Kendall's tau) | ☐ | x | Not a systematic review |
| | 15c | Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression) | ☐ | x | Not a systematic review |

| Section/topic | # | Checklist item | Information reported | | Line number(s) |
|---|---|---|---|---|---|
| | | | Yes | No | |
| | 15d | If quantitative synthesis is not appropriate, describe the type of summary planned | ☐ | x | Not a systematic review |
| **Meta-bias(es)** | 16 | Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies) | ☐ | x | Not a systematic review |
| **Confidence in cumulative evidence** | 17 | Describe how the strength of the body of evidence will be assessed (e.g., GRADE) | ☐ | x | Not a systematic review |

**Additional file 2. Pilot tests**

For our pilot studies we used the same sample of 14 reviews that was used for our pilot study of a previous protocol 'Seeking adverse effects in systematic reviews of orthodontic interventions: protocol for a cross-sectional study' [15]. The calculation of the sample size of this pilot study was based on the probability of the Yes scores for the question ''Did the review seek any findings related to adverse effects of interventions in the included studies? This sample size was calculated using we the following equation [29]:

$n = \frac{\ln(1-\Upsilon)}{\ln(1-\pi)}$

n = the sample size for the pilot study

ϒ = the threshold of confidence (95%)

π = the probability of a 'Yes' score

Our pilot test on our sample of 14 reviews found that reviewers in 35.7% (5/14) of the abstracts reported or considered (discussed, weighed etc.) potential adverse effects of orthodontic interventions. In this sample we identified a prevalence of 14.3 % (2/14) of spin in the abstract on adverse effects of orthodontic interventions. Both cases of spin were 'Misleading reporting related spin'.

**Additional file 3. Search terms and their derivatives**

This additional file is identical to additional file 3 of our protocol on seeking adverse in systematic reviews of orthodontic interventions [15].

**Table. Search terms and their derivatives**

| Search terms and their derivatives | Search terms for searching multiple words in a PDF |
|---|---|
| “adverse” | ADVERSE, Adverse, adverse |
| “effect”, “effects” | EFFECT, Effect, effect |
| “reaction”, “reactions” | REACTION, Reaction, reaction |
| “complication”, “complications”, “complicated”, “complicating” | COMPLICAT, Complicat, complicat |
| “harm”, “harms”, “harmful” | HARM, Harm, harm |
| “risk”, “risks”, “risky” | RISK, Risk, risk |
| “safe”, “safety” | SAFE, Safe, safe |
| “side” | SIDE, Side, side |
| “toxic”, “toxicity” | TOXIC, Toxic, toxic |
| “benefit”, “benefits” | BENEFIT, Benefit, benefit |
| “result”, “results” | RESULT, Result, result |
| “finding”, “findings” | FINDING, Finding, finding |
| “outcome”, “outcomes” | OUTCOME, Outcome, outcome |
| “limitation”, “limitations”, limit | LIMIT, Limit, limit |
| “damage”, “damages”, “damaging” | DAMAGE, Damage, damage |
| “data” | DATA, Data, data |
| “information” | INFO, Info, info |
| “conflict”, “conflicts”, “conflicting” | CONFLICT, Conflict, conflict |
| “negative” | NEGATIVE, Negative, negative |
| “detrimental” | DETRIMENTAL, Detrimental, detrimental |
| “disadvantage”, “disadvantages”, “disadvantageous” | DISADVAN, Disadvan, disadvan |
| “down” | DOWN, Down, down |
| “injury”, “injuries”, “injured”, “injurious” | INJUR, Injur, injur |
| “byproduct”, “byproducts” | BYPRODUCT, Byproduct, byproduct |
| “collateral” | COLLATERAL, Collateral, collateral |
| “unfavorable”, “unfavourable” | UNFAVO, Unfavo, unfavo |
| “destructive” | DESTRUCT, Destruct, destruct |
| “unsafe” | UNSAFE, Unsafe, unsafe |
| “undesired”, “undesirable” | UNDESIR, Undesir, undesir |
| “recommend”, “recommendation”, “recommending” | RECOMMEND, Recommend, recommend |
| “emergency”, “emergencies” | EMERGEN, Emergen, emergen |

## Additional file 4. Data collection forms

**Table 1. Data collection form to identify eligible reviews**

| Items | Description |
|---|---|
| Journal | List the pertinent journal |
| Year | Year of publication |
| Binder page number | List the binder page number |
| Reference | List full reference (Authors, Title, Journal) |
| Is the article a systematic review? | Answer: Yes/No<br>Consider definition of a systematic review |
| What type of systematic review? | List the type of systematic review.<br>Consider different types of systematic reviews.<br>When the publication is not an intervention systematic review describe what type it is or could be and classify. Types of systematic reviews will receive a final classification during the discussions between operators. |
| Were orthodontic interventions assessed? | Answer: Yes/No<br>Consider the definition of orthodontic interventions. |
| What was the orthodontic intervention? | List the type of orthodontic intervention<br>NA: When the article is not a systematic review or not a systematic review of interventions. |
| Is the systematic review eligible? | Answer: Yes/No<br>Yes: The article is a systematic review of an orthodontic intervention.<br>No: The article is not a systematic review of an orthodontic intervention.<br>No: The article is a systematic review of an orthodontic intervention, but focusses exclusively on its adverse effects. |
| Page and potential comments* | Present the pertinent pages of reference for scoring the previous items and list the potential comments. |

*When referring to a particular page in the systematic review, we will use the page number of the systematic review and not the number in the binder document.

**Table 2. Data collection form on seeking any findings related to adverse effects of interventions in the included studies**

| Items | Description |
|---|---|
| Did the review seek any findings related to adverse effects of interventions in the included studies? | Answer: Yes/No<br>Yes: Any findings related to adverse effects of interventions in the included studies were sought by the reviewers.<br>Seeking any findings related to adverse effects of interventions in the included studies refers to reporting anywhere in the review (except in the Abstract) that such adverse effects in the included studies were sought.<br>Yes: Yes is also scored when reviewers only reported findings related to adverse effects of interventions in the included studies, but did not report that they actually sought them or planned to seek them. For example 'Yes' will be scored when outcomes on adverse effects of interventions in the included studies were reported in the review, but were not defined as objectives of the review.<br>Yes: Yes is also scored when the reviewers reported that they planned to seek (for example in the research objectives) findings related to adverse effects of interventions in the included studies, but did not report on these findings.<br>No: Findings related to adverse effects of interventions in the included studies were not sought by the reviewers. |
| In abstracts of systematic reviews of orthodontic interventions were potential adverse effects of these interventions reported or considered (i.e., discussed, weighed etc.)? | Answer: Yes/No<br>Yes: In abstracts of systematic reviews of orthodontic interventions potential adverse effects of these interventions were reported or considered (i.e., discussed, weighed etc.).<br>No: In abstracts of systematic reviews of orthodontic interventions potential adverse effects of these interventions were not reported or considered (i.e., discussed, weighed etc.). |

**Table 3a. Data collection form to identify spin in reviews that did seek adverse effects of interventions**

| Items for misleading reporting (in the abstract) on adverse effects of interventions | Score |
|---|---|
| 1) Not reporting in the abstract on the results of the adverse effects that were reported in the main text of the review. | Yes/no |
| 2) Selective reporting in the abstract on the results of the adverse effects that were reported in the main text of the review. | Yes/no |
| *Summary score on the presence of misleading reporting (in the abstract) on adverse effects of interventions* | *Yes/no*<br>*Yes is scored when one or more of the 2 items is answered with a 'Yes'* |

| | |
|---|---|
| | *No is scored when both items are answered with a 'No'* |
| | |
| **Items for misleading interpretation (in the abstract) on adverse effects of interventions** | |
| 1) Claiming in the abstract that the intervention is safe (has no or minimal adverse effects), despite concerning results on the adverse effects in the main text of the review, e.g., based on non-statistically significant results on adverse effects with wide confidence intervals [17]. | Yes/no |
| 2) Downgrading in the abstract the importance of the adverse effects, despite concerning results on the adverse effects in the main text of the review. | Yes/no |
| 3) Recommendations are made in the abstract for clinical practice that are not congruent with the concerning results on the adverse effects in the main text of the review [17]. | Yes/no |
| *Summary score on the presence of misleading interpretation (in the abstract) on adverse effects of interventions* | *Yes/no*<br>*Yes is scored when one or more of the 3 items is answered with a 'Yes'*<br>*No is scored when all 3 items are answered with a 'No'* |
| | |
| **Items for misleading extrapolation (in the abstract) on adverse effects of interventions** | |
| 1) Results are extrapolated in the abstract to another population, intervention, outcome or setting than were assessed in the review despite evidence in the main text on concerning adverse effects on a different population, intervention, outcome or setting. | Yes/no |
| *Summary score on the presence of misleading extrapolation (in the abstract) on adverse effects of interventions* | *Yes/no*<br>*Yes is scored when the item is answered with a 'Yes'*<br>*No is scored when the item is answered with a 'No'* |

**Table 3b. Data collection form to identify spin in reviews that did not seek adverse effects of interventions**

| **Items for misleading reporting (in the abstract) on adverse effects of interventions** | **Score** |
|---|---|
| 1) Reporting on results of adverse effects in the abstract when adverse effects were not sought. | Yes/no |
| 2) Reporting in the abstract that adverse effects were sought when they were not sought. | Yes/no |
| *Summary score on the presence of misleading reporting (in the abstract) on adverse effects of interventions* | *Yes/no*<br>*Yes is scored when one or more of the 2 items is answered with a 'Yes'*<br>*No is scored when both items are answered with a 'No'* |
| | |
| **Items for misleading interpretation (in the abstract) on adverse effects of interventions** | |

| | |
|---|---|
| 1) Claiming in the abstract that the intervention is safe (has no or minimal adverse effects) despite not having sought adverse effects. | Yes/no |
| 2) Downgrading in the abstract the importance of the adverse effects, despite not having sought adverse effects. | Yes/no |
| 3) Recommendations are made in the abstract for clinical practice despite not having sought adverse effects. | Yes/no |
| *Summary score on the presence of misleading interpretation (in the abstract) on adverse effects of interventions* | *Yes/no*<br>*Yes is scored when one or more of the 3 items is answered with a 'Yes'*<br>*No is scored when all 3 items are answered with a 'No'* |
| | |
| **Items for misleading extrapolation (in the abstract) on adverse effects of interventions** | |
| 1) Results are extrapolated in the abstract to another population, intervention, outcome or setting than were assessed in the review despite not having sought adverse effects. | Yes/no |
| *Summary score on the presence of misleading extrapolation (in the abstract) on adverse effects of interventions* | *Yes/no*<br>*Yes is scored when the item is answered with a 'Yes'*<br>*No is scored when the item is answered with a 'No'* |

## Additional files chapter 5

**Additional file 1. STROBE Checklist**
STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

| | Item No | Recommendation | Page No |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 2 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 3-5 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 5 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 6 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6-9 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants | 6-8 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 9-10 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 10-11 |
| Bias | 9 | Describe any efforts to address potential sources of bias | NA |
| Study size | 10 | Explain how the study size was arrived at | 11-12 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 12 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 11-12 |
| | | (*b*) Describe any methods used to examine subgroups and interactions | 11-12 |
| | | (*c*) Explain how missing data were addressed | 11-12 |

| | | | |
|---|---|---|---|
| | | (*d*) If applicable, describe analytical methods taking account of sampling strategy | 11-12 |
| | | (*e*) Describe any sensitivity analyses | NA |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 13-15 |
| | | (b) Give reasons for non-participation at each stage | 13-15 |
| | | (c) Consider use of a flow diagram | 13 |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 13-15 |
| | | (b) Indicate number of participants with missing data for each variable of interest | 13-15 |
| Outcome data | 15* | Report numbers of outcome events or summary measures | 13-15 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 13-15 |
| | | (*b*) Report category boundaries when continuous variables were categorized | 13-15 |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | NA |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | NA |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 15 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 17 and 18 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 15-18 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 18 |
| **Other information** | | | |

| | | | |
|---|---|---|---|
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | NA |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

## Additional file 2

**Table of contents for additional file 2**

| Additional file item | Description |
|---|---|
| Additional file 2A | Differences between the protocol and the completed cross-sectional study |
| Additional file 2B | Search terms and their derivatives |
| Additional file 2C | Data collection forms |
| Additional file 2D | Adverse effects hypothetically linked to orthodontic interventions |
| References | References for additional file 2 |

**Additional file 2A. Differences between the protocol and the completed cross-sectional study**

| Differences between the protocol and the completed cross-sectional study | Rationale |
|---|---|
| Fine-tuning of the definitions of the 3 types of spin | In our protocol we wanted to identify spin by comparing what was reported in the abstract with what was reported in the main text of the manuscript. We changed this to comparing what was reported in the abstract with what was found in the review. This fine-tuning was necessary, because on a few occasions what was reported in the main text of the review was not completely congruent with the findings of the review or pertinent information was not reported in the main text of the review, but only in supplementary files. |
| Explorative analyses to assess the presence of spin in the abstract and a series of predictors | We assessed the association between the presence of spin in the abstract and a series of predictors. These predictors were not defined a priori in our protocol, but several were explored in recent studies on spin in the field of orthodontics (Guo 2021, Makou 2021). We therefore conducted explorative analyses to determine associations between the presence of spin in the abstract and various predictors. |

**Additional file 2B. Search terms and their derivatives**
**Table. Search terms and their derivatives**

| Search terms and their derivatives | Search terms for searching multiple words in a PDF |
|---|---|
| “adverse” | ADVERSE, Adverse, adverse |
| “effect”, “effects” | EFFECT, Effect, effect |
| “reaction”, “reactions” | REACTION, Reaction, reaction |
| “complication”, “complications”, “complicated”, “complicating” | COMPLICAT, Complicat, complicat |
| “harm”, “harms”, “harmful” | HARM, Harm, harm |
| “risk”, “risks”, “risky” | RISK, Risk, risk |
| “safe”, “safety” | SAFE, Safe, safe |
| “side” | SIDE, Side, side |
| “toxic”, “toxicity” | TOXIC, Toxic, toxic |
| “benefit”, “benefits” | BENEFIT, Benefit, benefit |
| “result”, “results” | RESULT, Result, result |
| “finding”, “findings” | FINDING, Finding, finding |
| “outcome”, “outcomes” | OUTCOME, Outcome, outcome |
| “limitation”, “limitations”, limit | LIMIT, Limit, limit |
| “damage”, “damages”, “damaging” | DAMAGE, Damage, damage |
| “data” | DATA, Data, data |
| “information” | INFO, Info, info |
| “conflict”, “conflicts”, “conflicting” | CONFLICT, Conflict, conflict |
| “negative” | NEGATIVE, Negative, negative |
| “detrimental” | DETRIMENTAL, Detrimental, detrimental |
| “disadvantage”, “disadvantages”, “disadvantageous” | DISADVAN, Disadvan, disadvan |
| “down” | DOWN, Down, down |
| “injury”, “injuries”, “injured”, “injurious” | INJUR, Injur, injur |
| “byproduct”, “byproducts” | BYPRODUCT, Byproduct, byproduct |
| “collateral” | COLLATERAL, Collateral, collateral |
| “unfavorable”, “unfavourable” | UNFAVO, Unfavo, unfavo |
| “destructive” | DESTRUCT, Destruct, destruct |
| “unsafe” | UNSAFE, Unsafe, unsafe |
| “undesired”, “undesirable” | UNDESIR, Undesir, undesir |
| “recommend”, “recommendation”, “recommending” | RECOMMEND, Recommend, recommend |
| “emergency”, “emergencies” | EMERGEN, Emergen, emergen |

**Additional file 2C. Data collection forms**

**Data collection form on reporting of adverse effects in the abstract of systematic reviews of orthodontic interventions**

| Items | Description |
|---|---|
| Did the review seek any findings related to adverse effects of interventions in the included studies? | Answer: Yes/No<br>Yes: Any findings related to adverse effects of interventions in the included studies were sought by the reviewers.<br>Seeking any findings related to adverse effects of interventions in the included studies refers to reporting anywhere in the review (except in the Abstract) that such adverse effects in the included studies were sought.<br>Yes: Yes is also scored when reviewers only reported findings related to adverse effects of interventions in the included studies, but did not report that they actually sought them or planned to seek them. For example 'Yes' will be scored when outcomes on adverse effects of interventions in the included studies were reported in the review, but were not defined as objectives of the review.<br>Yes: Yes is also scored when the reviewers reported that they planned to seek (for example in the research objectives) findings related to adverse effects of interventions in the included studies, but did not report on these findings.<br>No: Findings related to adverse effects of interventions in the included studies were not sought by the reviewers. |
| In abstracts of systematic reviews of orthodontic interventions were potential adverse effects of these interventions reported or considered (i.e., discussed, weighed etc.)? | Answer: Yes/No<br>Yes: In abstracts of systematic reviews of orthodontic interventions potential adverse effects of these interventions were reported or considered (i.e., discussed, weighed etc.).<br>No: In abstracts of systematic reviews of orthodontic interventions potential adverse effects of these interventions were not reported or considered (i.e., discussed, weighed etc.). |

**Data collection forms to identify spin of adverse effects of orthodontic interventions in abstracts of systematic reviews**

To assign spin of adverse effects of orthodontic interventions in abstracts of systematic reviews we developed separate checklists for reviews that sought adverse effects of interventions and those that did not. These checklists were pilot-tested a priori during the development of our protocol. Because only 2 systematic reviews in this pilot study reported on adverse effects of interventions, we decided to conduct an additional pilot test to further fine-tune these checklists. Ten randomized controlled trials (RCTs) (2 per journal) of orthodontic interventions were selected consecutively from the websites of the 5 leading orthodontic journals from June 2021 backwards. RCTs were eligible for the pilot study if they assessed adverse effects of orthodontic interventions. The first 2 RCTs for each journal that were identified during this search process were selected. The fine-tuned checklists are reported in the tables under here and differ slightly from those reported in our protocol (Steegmans 2019). Changes were made to (1) reduce inter-operator differences in assigning various types of spin and (2) make the descriptions of spin more congruent with those given in the literature (Boutron 2018, Haneef 2017, Lazarus 2015) and with the definition of spin (in the abstract) on adverse effects of interventions presented in our protocol (Steegmans 2019), i.e., 'Incomplete or inadequate reporting, interpretation, or extrapolation (or a combination of these variables) of findings on adverse effects of interventions in the abstract that could be misleading for the reader'(See additional file 2A).

**Data collection form to identify spin in abstracts of reviews that did seek adverse effects of interventions**

| **Items for misleading reporting (in the abstract) on adverse effects of interventions** | **Score** |
|---|---|
| 1) Not reporting in the abstract on the results of adverse effects found in the review. | Yes/no |
| 2) Selective reporting in the abstract on the results of adverse effects found in the review. | Yes/no |
| *Summary score on the presence of misleading reporting (in the abstract) on adverse effects of interventions* | *Yes/no*<br>*Yes is scored when one or more of the 2 items is answered with a 'Yes'*<br>*No is scored when both items are answered with a 'No'* |
| | |
| **Items for misleading interpretation (in the abstract) on adverse effects of interventions** | |
| 1) Claiming in the abstract that the intervention is safe (has no or minimal adverse effects), despite concerning results on adverse effects found in the review e.g., based on non-statistically significant results on adverse effects with wide confidence intervals (Yavchitz 2016) | Yes/no |
| 2) Downgrading in the abstract the importance of the adverse effects, despite concerning results on adverse effects found in the review. | Yes/no |
| 3) Recommendations are made in the abstract for clinical practice that are not supported by the findings in the review on adverse effects'(Yavchitz 2016) | Yes/no |
| *Summary score on the presence of misleading interpretation (in the abstract) on adverse effects of interventions* | *Yes/no*<br>*Yes is scored when one or more of the 3 items is answered with a 'Yes'*<br>*No is scored when all 3 items are answered with a 'No'* |
| | |
| **Items for misleading extrapolation (in the abstract) on adverse effects of interventions** | |
| 1) Results are extrapolated in the abstract to another population, intervention, outcome or setting than were assessed in the review despite evidence on adverse effects on a different population, intervention, outcome or setting. | Yes/no |
| *Summary score on the presence of misleading extrapolation (in the abstract) on adverse effects of interventions* | *Yes/no*<br>*Yes is scored when the item is answered with a 'Yes'*<br>*No is scored when the item is answered with a 'No'* |

**Data collection forms to identify spin in abstracts of reviews that did not seek adverse effects of interventions**

| **Items for misleading reporting (in the abstract) on adverse effects of interventions** | **Score** |
|---|---|
| 1) Reporting on results of adverse effects in the abstract when adverse effects were not sought. | Yes/no |
| 2) Reporting in the abstract that adverse effects were sought when they were not sought. | Yes/no |
| *Summary score on the presence of misleading reporting (in the abstract) on adverse effects of interventions* | *Yes/no*<br>*Yes is scored when one or more of the 2 items is answered with a 'Yes'*<br>*No is scored when both items are answered with a 'No'* |
| | |
| **Items for misleading interpretation (in the abstract) on adverse effects of interventions** | |
| 1) Claiming in the abstract that the intervention is safe (has no or minimal adverse effects) despite not having sought adverse effects. | Yes/no |
| 2) Downgrading in the abstract the importance of the adverse effects, despite not having sought adverse effects. | Yes/no |
| 3) Recommendations are made in the abstract for clinical practice despite not having sought adverse effects. | Yes/no |
| *Summary score on the presence of misleading interpretation (in the abstract) on adverse effects of interventions* | *Yes/no*<br>*Yes is scored when one or more of the 3 items is answered with a 'Yes'*<br>*No is scored when all 3 items are answered with a 'No'* |
| | |
| **Items for misleading extrapolation (in the abstract) on adverse effects of interventions** | |
| 1) Results are extrapolated in the abstract to another population, intervention, outcome or setting than were assessed in the review despite not having sought adverse effects. | Yes/no |
| *Summary score on the presence of misleading extrapolation (in the abstract) on adverse effects of interventions* | *Yes/no*<br>*Yes is scored when the item is answered with a 'Yes'*<br>*No is scored when the item is answered with a 'No'* |

**Additional file 2D. Adverse effects hypothetically linked to orthodontic interventions (Steegmans 2023a)**

| Adverse effects related to | Description |
|---|---|
| Tooth structures | Tooth crown<br>• decalcifications, decays, tooth wear, enamel cracks and fractures; discolorations, deterioration of prosthetic crown (as fracturing a ceramic one during debonding);<br>• iatrogenic damage to the crown, e.g., fracture as a result of trauma<br>Tooth root<br>• root resorption, early closure of root apex, ankylosis;<br>• iatrogenic damage to the root, e.g., fracture as a result of trauma<br>Tooth pulp<br>• ischemia, pulpitis, necrosis<br>• iatrogenic damage to the pulp, e.g., fracture as a result of trauma |
| Periodontal tissues | • gingivitis, periodontitis, gingival recession or hypertrophy, alveolar bone loss, dehiscences, fenestrations, interdental fold, dark triangles; tooth mobility, plague retention, bacterial count |
| Intraoral (non-tooth or periodontal) tissues | • intraoral tissue irritations and inflammation such as mucosal ulcerations or hyperplasia or irritations of the tongue (as a result of trauma by appliances, e.g., breakage, failure, loosening etc. of appliances or long arch wires)<br>• Scar formation after suturing<br>• chemical burns (e.g., etching related)<br>• thermal injuries (e.g., overheated burs)<br>• nerve damage<br>• tooth eruption, i.e., eruption disturbances (e.g., impactions) caused by orthodontic appliances |
| Extraoral tissues (non-temporomandibular tissues) | • cutting of lips or cheeks, eye injury (e.g., as a result of trauma by appliances, e.g., breakage, failure, loosening etc. of appliances or long arch wires or headgear-related trauma)<br>• discomfort on the lip |
| Temporomandibular tissues and disorders | • temporomandibular tissues and disorders |
| Appliance failure | • breakage, failure, loosening etc. of appliances<br>• long archwires, headgear-related trauma |
| Undesired treatment results | • inadequate morpho-functional, aesthetic or functional final result<br>• inaccuracy of the treatment result<br>• non predictability of the treatment result<br>• Dental side effects e.g., unwanted tipping of teeth, anchorage loss etc.<br>• Skeletal side effects, e.g., unwanted backward rotation of the mandible |
| Relapse and stability | • Relapse and stability of the obtained treatment result |
| Undesired qualitative experiences by the patient or carer(s) | Pain and discomfort<br>• orthodontic tooth movement-related pain and discomfort<br>• appliance (intervention)-related pain and discomfort: i.e., pain and discomfort as a result of the appliance (intervention) itself with or without pain and discomfort associated with tooth movement e.g., tension or pressure of the appliances (constriction of appliances), speech difficulties, eating difficulties, swallowing difficulties, food accumulation, bad tastes and smells<br>• additional intervention-related pain and discomfort, e.g., surgical and non-surgical adjunctive interventions to accelerate tooth movement<br>Tolerability/acceptance/stress issues with the treatment procedures<br>• Absence from work or studies and difficulties in daily activities<br>• collaboration (compliance) issues or failure to complete treatment, e.g., dropout |

| | |
|---|---|
| | • patient anxiety<br>• being teased<br>• social discomfort<br>• embarrassment to wear the appliance<br>• behavioral changes of patients and parents, impaired family relationships<br>• aesthetic look discontents during orthodontic appliance usage<br>• concentration difficulties<br>• reduced enjoyment of food and change in taste<br>• sleeping difficulties<br>• removal of appliance during sleep<br>• development of mannerisms<br>Satisfaction with the treatment procedures and final result<br>• not satisfied with the treatment procedures (Check in text what was measured, i.e., during or after)<br>• not satisfied with the final treatment result (Check in text what was measured, i.e., during or after) |
| Gastro-intestinal | • accidental swallowing of small parts of the orthodontic device (tubes, brackets); |
| Allergy | • Allergies to nickel or latex; |
| Cardio | • infective endocarditis; |
| Chronic fatigue | |
| Cross infections | • from doctor to patient, patient to doctor, patient to patient. |
| Non-defined | Adverse effects that were not defined by the authors of the review: referring to 'any adverse effect', 'any side effect' etc. |
| Additional adverse effects | Additional adverse effects that were identified during data extraction that could not be labeled under any of the categories of adverse effects given in this table |

*Modified from Preoteasa et al. (Preoteasa 2012)

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**Steegmans 2019**
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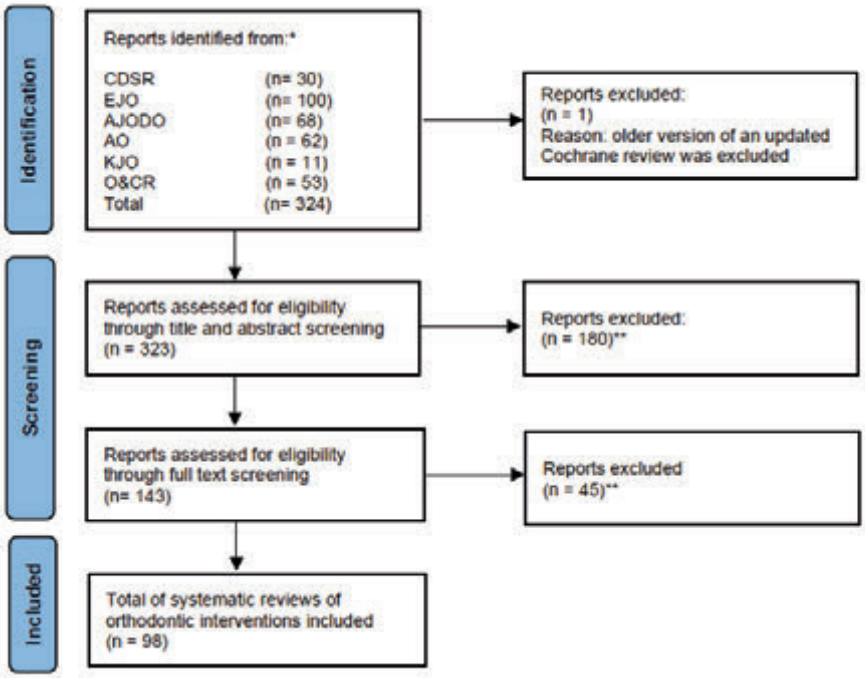
**Yavchitz 2016**
Yavchitz A, Ravaud P, Altman DG, Moher D, Hrobjartsson A, Lasserson T, Boutron I. A new classification of spin in systematic reviews and meta-analyses was developed and ranked according to the severity. J Clin Epidemiol. 2016 Jul;75:56-65. doi: 10.1016/j.jclinepi.2016.01.020. Epub 2016 Feb 2.

## Additional file 3

**Table of contents for additional file 3**

| Additional file item | Description |
|---|---|
| Additional file 3A | PRISMA flow diagram |
| Additional file 3B | Included reviews |
| Additional file 3C | Excluded studies with rationale |

### Additional file 3A. PRISMA flow diagram




*CDSR: Cochrane Database of Systematic Reviews, EJO: European Journal of Orthodontics, AJODO: American Journal of Orthodontics and Dentofacial Orthopedics, AO: Angle Orthodontist,
KJO: Korean Journal of Orthodontics, O&CR: Orthodontics and Craniofacial Research
** The rationale for exclusion of each report are given in Additional file 3C

### Additional file 3B. Included reviews

This additional file is identical to additional file 3 of chapter 3.

### Additional file 3C. Excluded studies with rationale

This additional file is identical to additional file 4 of chapter 3.

# Additional files chapter 8

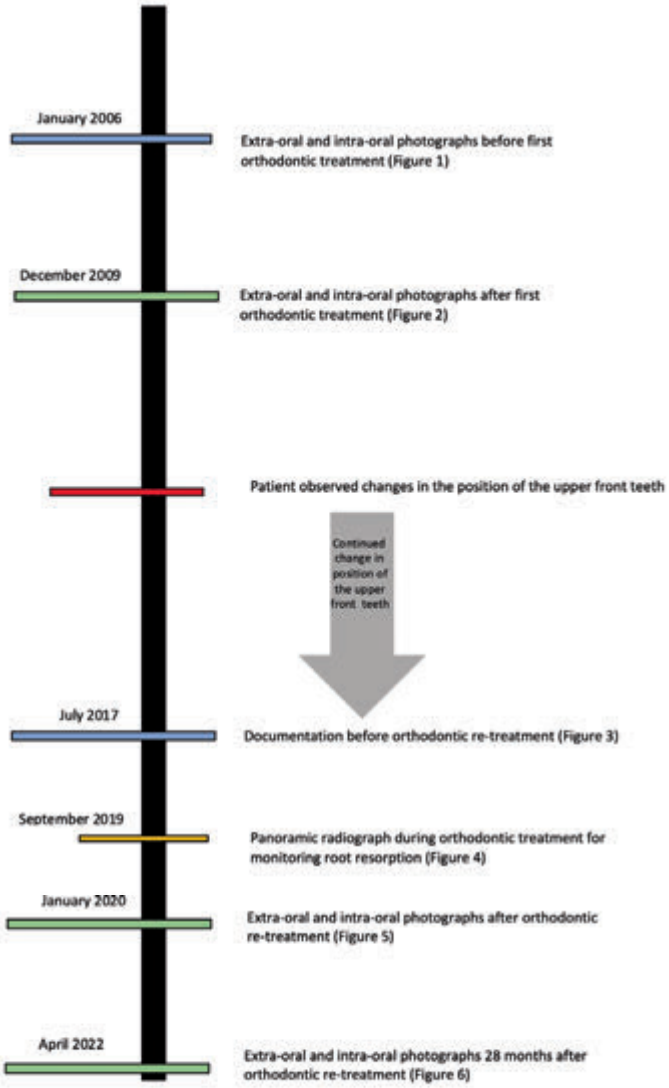
**Additional file 1. CARE Checklist**

CARE case report guidelines

**CARE Checklist of information to include when writing a case report**

| Topic | Item | Checklist item description | Reported on Line |
|---|---|---|---|
| **Title** | 1 | The diagnosis or intervention of primary focus followed by the words "case report" | P1 |
| **Key Words** | 2 | 2 to 5 key words that identify diagnoses or interventions in this case report, including "case report" | P1 |
| **Abstract (no references)** | 3a | Introduction: What is unique about this case and what does it add to the scientific literature? | P1 |
| | 3b | Main symptoms and/or important clinical findings | P1 |
| | 3c | The main diagnoses, therapeutic interventions, and outcomes | P1 |
| | 3d | Conclusion—What is the main "take-away" lesson(s) from this case? | P1 |
| **Introduction** | 4 | One or two paragraphs summarizing why this case is unique **(may include references)** | P1-2 |
| **Patient Information** | 5a | De-identified patient specific information | P2-3 |
| | 5b | Primary concerns and symptoms of the patient | P3 |
| | 5c | Medical, family, and psycho-social history including relevant genetic information | P3 |
| | 5d | Relevant past interventions with outcomes | P3 |
| **Clinical Findings** | 6 | Describe significant physical examination (PE) and important clinical findings | P4 |
| **Timeline** | 7 | Historical and current information from this episode of care organized as a timeline | P4 |
| **Diagnostic Assessment** | 8a | Diagnostic testing (such as PE, laboratory testing, imaging, surveys). | P5-6 |
| | 8b | Diagnostic challenges (such as access to testing, financial, or cultural) | P5-6 |
| | 8c | Diagnosis (including other diagnoses considered) | P6 |
| | 8d | Prognosis (such as staging in oncology) where applicable | P6 |
| **Therapeutic Intervention** | 9a | Types of therapeutic intervention (such as pharmacologic, surgical, preventive, self-care) | P6-7 |
| | 9b | Administration of therapeutic intervention (such as dosage, strength, duration) | P6-7 |
| | 9c | Changes in therapeutic intervention (with rationale) | P6-7 |
| **Follow-up and Outcomes** | 10a | Clinician and patient-assessed outcomes (if available) | P8 |
| | 10b | Important follow-up diagnostic and other test results | P9 |
| | 10c | Intervention adherence and tolerability (How was this assessed?) | P9 |
| | 10d | Adverse and unanticipated events | P9 |
| **Discussion** | 11a | A scientific discussion of the strengths AND limitations associated with this case report | P10 |
| | 11b | Discussion of the relevant medical literature **with references** | P10 |
| | 11c | The scientific rationale for any conclusions (including assessment of possible causes) | P11 |
| | 11d | The primary "take-away" lessons of this case report (without references) in a one paragraph conclusion | P11 |
| **Patient Perspective** | 12 | The patient should share their perspective in one to two paragraphs on the treatment(s) they received | P3 |
| **Informed Consent** | 13 | Did the patient give informed consent? Please provide if requested | **Yes** |

**Additional file 2**




**Supplementary file 2**. Timeline

**Additional file 3**

# Orthodontie

ACTA ACADEMISCH CENTRUM TANDHEELKUNDE AMSTERDAM

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Tel: 020- 5980610 / 5980611

**UW geboorte datum:**
**geslacht M/V**
**NAAM van uw behandelaar:**
ESASnummer:
https://esas.nu/

## Patiënten enquête Esas 2019 2020

**datum :** 22 / 01 / 2020

Geachte ouders en patiënt(e),
Wij doen ons best om op een prettige manier goede orthodontische zorg te verlenen, rekening houdend met de wensen en de verwachtingen van onze patiënten. Om na te gaan of dat lukt, worden zowel patiënten als ouders verzocht hun mening over onze afdeling te geven, via het invullen van deze enquête. Met de resultaten hiervan kunnen wij werken aan verbetering van onze zorgverlening. U hoeft uw naam niet te vermelden, want het onderzoek is gegarandeerd anoniem. Wij stellen het bijzonder op prijs als ook u hieraan wilt meewerken, het duurt slecht enkele minuten. Bij voorbaat hartelijk dank voor uw moeite en tijd om onze praktijkorganisatie mede door uw input te verbeteren.

| A **Over de orthodontist** | **niet waar ← → wel waar** |
|---|---|
| 1. Is vriendelijk en goed aanspreekbaar | ○ ○ ○ ○ ✕ |
| 2. Houdt me goed op de hoogte van het verloop van de behandeling | ○ ○ ○ ○ ✕ |
| 3. Heeft mijn volledige vertrouwen | ○ ○ ○ ○ ✕ |
| 4. Geeft mij alle informatie die ik nodig heb | ○ ○ ○ ○ ✕ |
| 5. Neemt de tijd voor me | ○ ○ ○ ○ ✕ |
| 6. Luistert naar wat ik te zeggen heb | ○ ○ ○ ○ ✕ |
| 7. Is helder en duidelijk | ○ ○ ○ ○ ✕ |
| 8. Gaat goed om met mensen | ○ ○ ○ ○ ✕ |
| 9. Werkt netjes op tijd | ○ ○ ○ ○ ✕ |
| 10. Is goed in wat hij/zij doet | ○ ○ ○ ○ ✕ |

| B **Over de praktijkmedewerk(st ) ers** | **niet waar ← → wel waar** |
|---|---|
| 11. Zijn vriendelijk | ○ ○ ○ ○ ✕ |
| 12. Zijn zorgzaam en plezierig | ○ ○ ○ ○ ✕ |

## Orthodontie

| | |
|---|---|
| 13. Vormen een goed team | ○ ○ ○ ○ ✕ |
| 14. Zijn goed in wat zij doen | ○ ○ ○ ○ ✕ |
| 15. De telefoon wordt prompt beantwoord | ○ ○ ○ ○ ✕ |
| 16. Afspraken maken gaat gemakkelijk en snel | ○ ○ ○ ○ ✕ |
| **C Over de praktijk** | |
| 17. De praktijk ziet er goed uit | ○ ○ ○ ○ ✕ |
| 18. De wachtkamer is aangenaam | ○ ○ ✕ ○ ○ |
| 19. Er zijn altijd voldoende nieuwe tijdschriften aanwezig | ○ ○ ✕ ○ ○ |
| 20. De praktijk is goed bereikbaar | ○ ○ ○ ✕ ○ |
| **D Over de behandeling** | **niet waar ← → wel waar** |
| 21. Ik heb nooit iets echt vervelends ervaren | ○ ○ ○ ○ ✕ |
| 22. Het eindresultaat is zoals ik had verwacht | ○ ○ ○ ○ ✕ |
| 23. De behandeling duurde net zo lang als was voorspeld | ○ ○ ○ ✕ ○ |
| 24. Mijn tanden zijn heel mooi geworden | ○ ○ ○ ○ ✕ |
| **E Tenslotte** | |
| 25. Ik zal deze praktijk aan mijn vrienden aanbevelen | ○ ○ ○ ✕ |

**Supplementary file 3**. ESAS patient satisfaction evaluation part