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PROGRESSION OF VOLUMETRIC AND SURFACE TOOTH WEAR IN PATIENTS HAVING UNDERGONE ORTHODONTIC TREATMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

PROGRESSION OF VOLUMETRIC AND SURFACE TOOTH WEAR IN PATIENTS HAVING UNDERGONE ORTHODONTIC TREATMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Aim: Tooth surface loss additional to the physiologic alterations of the dentition, may occur during orthodontic treatment due to interferences and functional changes, abrasion by orthodontic appliances and other factors. The aim of this study was to investigate systematically the relevant literature on the progression of volumetric and surface tooth wear in patients having undergone comprehensive orthodontic treatment.

Materials and Methods: Search without restrictions for published and unpublished literature and hand searching took place. Data on volumetric and surface tooth wear in patients having undergone comprehensive orthodontic treatment were reviewed and the risk of bias was assessed using the ROBINS-I tool. The random effects method was used to synthesize results, where appropriate, and the Grades of Recommendation, Assessment, Development and Evaluation approach assessed the quality of evidence (confidence in the observed estimates).

Results: Three studies met the inclusion criteria from the initial 4,389 identified from the database search. Two studies assessed tooth surface loss using 3D volumetric measurements and one used grading scales. All three studies were deemed to have a serious risk of bias and reported surface loss. Of the two studies that assessed volumetric change, one measured the canines only and the other assessed three groups of teeth; incisors, canines and posterior teeth (premolars and molars). From these two studies the overall mean volume reduction in 342 canines was 1.62 mm^3 [95% Confidence Interval (CI): 0.87 – 2.38] in 86 participants [I^2 = 96%]. The volumetric change in 194 incisors was 1.02 mm^3 [95% CI: 0.84 – 1.20] and for the 316 posterior teeth it was 0.95 mm^3 [95% CI: 0.84 – 1.07] in 30 participants. The overall quality of evidence limited the confidence in the observed estimates.

Conclusions: Varying degrees of tooth surface loss occurred after comprehensive orthodontic treatment. Further studies are needed in order to elucidate how much of the reduction is directly associated with orthodontic treatment and how much is due to physiologic tooth wear.

DEDICATION

With great gratitude and appreciation, I would like to dedicate this thesis to my beloved parents, who have always stood by my side.

DECLARATION

I declare that all the content of the thesis is my own work. There is no conflict of interest with any other entity or organization.

Name: Miltiadis A. Makrygiannakis

Signature:

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1. INTRODUCTION

The aim of orthodontic treatment is to result in a long-term healthy, esthetic and functional occlusion. In general, there are six main indications for orthodontic treatment (Proffit et al., 2007):

a) elimination or alleviation of a possible social handicap, by ameliorating dental and/ or facial appearance,

b) further enhancement of dental and facial appearance in individuals whose appearance is already acceptable,

c) normalization, to the extent possible, of developmental processes, during the periods of dentofacial growth and development of the dentition,

d) functional improvement and elimination of functional impairments, if any,

e) alleviating the consequences of trauma or disease,

f) being part of an interdisciplinary adjunctive treatment.

Despite the benefits of orthodontics, sometimes undesirable iatrogenic adverse effects may occur to soft or hard tissues, such as enamel surface changes associated with the procedures of bonding and removal of the appliances, or observed during the course of treatment, enamel color changes, root resorption, decalcifications, bone dehiscence or fenestration and effects on the periodontal tissues (Graber et al., 2004; Justus, 2015).

One of the undesirable consequences of orthodontic therapy is occlusal wear. It is defined as “the loss of substance on opposing occlusal units or surfaces as the result of attrition or abrasion” (Glossary of Prosthodontic Terms, 2017). Although it has been reported that tooth wear occurs regardless of orthodontic treatment (Mwangi et al., 2009), tooth surface loss in addition to normal physiologic alterations of the dentition may occur due to interferences and functional changes, abrasion by appliances and other factors (Dahl et al., 1985, Øgaard et al., 2004). Apart from special references concerning the instigation of excessive tooth wear by ceramic brackets when they come into contact with the opposing teeth (Douglass, 1989; Viazis et al., 1990; Bishara and Dale, 1997), possible associations of tooth surface loss during orthodontic treatment have originated mainly from other aspects of the therapy itself. Nevertheless, the relevant data seem to be not only limited, but inconsistent (Øgaard et al., 2004). The aim of the present study was to systematically investigate and critically appraise the quality of the available evidence regarding the progression of volumetric and surface tooth wear in patients after having undergone comprehensive orthodontic treatment.

2. REVIEW OF THE LITERATURE

Particular interest about the side effects of orthodontic treatment, whether existing or hypothesized, has increased during the last few years (Graber et al., 2004; Justus, 2015). However, the association of an untoward effect with orthodontic treatment, or a demonstration of the causative mechanism is not always simple to substantiate, mainly because of the complexity involved in the instigation of such side effects, individual variations, and problematic nature of the methodology of investigating a cause-effect relationship.

2.1. Classification of the iatrogenic effects of associated with orthodontic treatment

In general, the iatrogenic effects associated with orthodontic treatment can be classified, according to their localization, as systemic or localized.

2.1.1. Systemic side effects

Two different possible systemic side effects of orthodontic treatment have been discussed in the available literature: a) allergic reaction to material components (usually, latex or nickel), and b) release of wear and corrosion products from orthodontic alloys (Graber et al., 2004).

a) Allergic reaction to material components

Many medical products contain natural rubber latex (NRL) among their constituents. The patients that have been sensitized to NRL are more likely to suffer from allergic reactions. They usually present with delayed symptoms such as a localized red itchy rash, or with immediate symptoms such as itching of the skin and eyes, sneezing, bronchospasm or anaphylactic shock (McEntee, 2012). The available data indicate two types of allergic reactions associated with orthodontic treatment: Type I and Type IV. The former is characterized by an immediate antibody mediated allergic response. It takes place within minutes or hours after direct exposure of the allergen to the skin or mucosa. The latter consists of a delayed hypersensitivity reaction that is usually diagnosed as a localized allergic contact dermatitis. Among its symptoms are diffuse or patchy eczema on the contact area, sometimes combined with itching, redness, and vesicle formation. Despite the nature of these reactions is not usually fatal, they can still cause serious health impact, if not treated (Patel et al., 2009).

In the case of latex allergy, both types of reaction may happen. Their prevalence differs between the general population and dental professionals with values of less than 1% and 6-12% respectively (Patel et al., 2009). The main risk factors for the development of such an allergy are a history of asthma, contact dermatitis, eczema, hay fever, penicillin allergy, and spina bifida (American Dental Association Council on Scientific Affairs, 1999; Guggenheimer et al., 2012). In addition to this, the occurrence of allergy to fruits such as avocado, banana, chestnut and, passion fruit may also stipulate a potential allergy to latex as well. The abovementioned fruit proteins have the capacity to cross-react with latex proteins and therefore participate in sensitization of the host to latex (Hain et al., 2007). Nevertheless, a final diagnosis is made depending on medical history and a positive skin reaction to specific chemicals existing in latex (Patel et al., 2009).

Regarding nickel allergy, nickel titanium archwires primarily, and stainless steel archwires, bands and brackets secondarily, are the materials exposing the patient to the risk of nickel leakage, and thus, allergy (Patel et al., 2009). The response is usually a type IV reaction. The increase in sensitization to nickel has been proportional to the increase in the use of jewelry containing the metal (Patel et al., 2009). The prevalence of nickel allergy has been reported to be 9.8% among Swedish women aged 16–19 years in 2011–2013, and 14–18% in adults of both sexes in other EU countries in 2008–2011 (Ahlström et al., 2017). Clinical signs and symptoms include angular cheilitis, a burning sensation, erythema multiforme, gingival hyperplasia, labial desquamation, loss of taste or a metallic taste, numbness and soreness of the tongue (Noble et al., 2008). Nevertheless, a recent in vitro study showed that the daily nickel release of Nickel-Titanium (NiTi), Stainless Steel (SS), Copper-Nickel-Titanium (CuNiTi) and ion implanted Nickel-Titanium by orthodontic appliances, in an acid pH, particularly favorable to corrosion, was found to be reduced in relation to that ingested with a normal daily diet. Therefore, the magnitude of the quantities of metal ions released in the experimental conditions should not be a reason for concern in utilizing the appliance (Senkutvan et al., 2014).

In fact, most individuals allergic to nickel do not exhibit reactions to nickel containing orthodontic materials, possibly due to a higher concentration of nickel necessary to initiate immune response in the oral mucosal environment compared with skin (Patel et al., 2009). In addition, orthodontic treatment has not been proven to be associated with an increase in the prevalence of nickel hypersensitivity unless the subjects had a history of cutaneous piercing (Kolokitha et al., 2008).

b) Release of wear and corrosion products from orthodontic alloys

Another undesirable systemic side-effect of orthodontic treatment is the release of wear and corrosion products from orthodontic alloys. Corrosion occurs in the oral environment, independent of their metallurgical structure and is accelerated by the inevitable surface defects (Eliades et al., 2004).

Several types have been reported in the literature. Pitting corrosion has been detected in brackets and wires. On the other hand, crevice corrosion is mainly found in restricted spaces, sometimes through the application of elastomeric ligatures on a bracket, and arises from differences in metal ion and oxygen concentration between the crevice and its surroundings. Last but not least, fretting corrosion, which occurs during sliding of a metallic wire on the slot of a bracket, with the underlying mechanism involving cold welding at the interfaces under pressure, causes rupture of the contact points (Eliades et al., 2004).

The main corrosion products of stainless steel are iron, chromium and nickel. Among them, nickel and chromium have drawn most of the attention because of their potential allergic, toxic and carcinogenic effects (Eliades et al., 2004).

In general, solutions of nickel (0.05 μmol/L) and cobalt (0.01 μmol/ L) have been shown to undermine phagocytosis of bacteria by polymorphonuclear leucocytes. The mechanism through which this process takes place is by influencing the chemotaxis of leucocytes, mediated by a change in shape. At the same time, neutrophils are stimulated to become aspherical, move more slowly and prevent calcium-ion contractile activity (Wataha et al., 1999).

In addition, nickel complexes in the form of arsenides and sulfides have been classified as carcinogens, allergens, and mutagens. Nickel is capable of mimicking hypoxia by upregulating Cap43, a hypoxia-regulated gene. Nevertheless, another relevant theory involves the formation of acetaldeyde in combination with oxidizing action, displayed by the increase in lactoferin receptors following exposure to the metal (Eliades et al., 2004).

Finally, it has been demonstrated that site-specific DNA base damage, single-strand scission, microsatellite mutations, inhibition of nucleotide repair and increase of total genomic methylation can take place at nontoxic concentrations. All these contributions can lead to genetic instability (Lee et al., 1998; Lloyd et al., 1999).

2.1.2. Localized side effects

The localized side effects of orthodontic treatment have been usually categorized as either adverse effects related to tooth-supporting tissues or adverse effects on dental tissues.

a) Adverse effects related to tooth-supporting tissues

The initiating, and most important, factor in gingival inflammation is the presence of bacterial plaque at the gingival margin. Specifically, orthodontic patients with fixed appliances demonstrate an increased tendency to accumulate microbial species responsible for the development of gingivitis. Fixed orthodontic appliances may lead to a rapid increase in the volume of dental plaque which is associated with a lower resting pH than that of non-orthodontic subjects (Chatterjee and Kleinberg, 1979; Gwinnett and Ceen, 1979). Many factors may have an additional effect on the distribution of biofilm in patients wearing fixed appliances. A recent study found that the highest accumulation occurred on the maxillary lateral incisors and maxillary canines, particularly in the gingival area and areas behind arch wires, while female subjects and adult patients presented the least accumulation (Mei et al., 2017). In addition, it has been demonstrated that three months after the removal of appliances, the periodontal changes induced by orthodontic therapy are only partially reversed. The prevalence and counts of periodontopathogens tended to be normal, but probing depth and the amount of Prevotella intermedia were still significantly higher for the group that had undergone orthodontic treatment (Pan et al., 2017).

Alveolar bone height loss has a multifactorial etiology when in conjunction with orthodontic treatment. A study that examined the prevalence and the changes in marginal bone support in orthodontically treated maxillary dental arches compared to the untreated mandibular, showed that the reduction in marginal bone was greater for the maxilla in relation to the mandible, although little or no damage at all was manifested in the majority of cases (Hollender et al., 1980). Changes in alveolar bone height and cortical bone thickness may also occur around the lower incisors. However, incisor inclination was not correlated with alveolar bone height changes (Garlock et al., 2016).

In general, it is accepted that orthodontic treatment per se*,* is not considered as inducing bone destruction (Thilander, 2004), although small detrimental effects to the periodontium have been reported (Bollen et al., 2008), especially in cases with thin gingival biotype and labially displaced roots (Chaushu and Stabholz, 2013). However, under specific situations, further periodontal tissue deterioration may occur. Tipping forces might shift plaque from a supragingival to a subgingival position and thus contribute to the creation of infrabony pocket defects (Ericsson et al., 1977). Moreover, problems like dehiscences, fenestrations and recessions might occur due to uncontrolled labial or buccal tooth movements. In contrast to fenestration, which occurs mainly in the apical part of the root, a bone dehiscence involves marginal bone loss at either the labial or buccal part of the root (Thilander, 2004). Finally, patients undergoing rapid maxillary expansion while their palatal sutures are completely or partially closed are at a higher risk of tipping or tilting of the premolars and molars towards the cortical bone and thus potential damage to the periodontal tissues (Thilander, 2004). However, despite greater amounts of maxillary expansion during treatment, the effects are still minimal (Morris et al., 2017).

b) Adverse effects on dental tissues

Root resorption

Although cementum shows a higher resistance to resorption than alveolar bone, the application of forces may have an impact on both cementum and dentine. Presently, there is no consensus regarding this matter. The associated factors are considered to be both biological and mechanical (Brezniak and Wasserstein, 2002).

According to some authors, resorption results from a richer blood supply adjacent to the alveolar bone than to the cementum (Khouw and Goldhaber, 1990). Other parameters that have been implicated in the greater prevalence of root resorption during orthodontic treatment are: individual susceptibility (Harris et al., 1997), gender (Linge and Linge, 1983), pre-existing inflammatory conditions (Davidovitch et al., 1995), hormonal imbalances (i.e., hypothyroidism, hypopituitarism, hyperpituitarism) (Engstrom et al., 1988), advanced age (Reitan et al., 1994), pre-existing resorption (Goldson et al., 1975), dental anomalies (i.e., ectopia, agenesis, taurodontism) (Kjaer, 1995), oral habits (Odenrick et al., 1985), existence of an open bite (Motokawa et al., 2013), movement into cortical or labial bone (Malmgren et al., 1994), trauma to the teeth (Andreasen, 1988; Malmegren et al., 1982), occlusal trauma (Cakmak et al. 2014), increased magnitude of forces (Kvam,1967; Harry and Sims, 1982; Vardimon et al., 1991; Eross et al., 2015), the use of intermaxilary elastics (Linge and Linge, 1983) and the application of continuous forces (Levander and Malmgren, 1994).

Alterations to enamel surface

Orthodontic treatment may impact on the enamel surface from the beginning to the the end. Enamel surface changes associated with the procedures of bonding and removal of the appliances, or observed during the course of treatment (surface wear or decalcification), as well as enamel color changes have all been reported.

During bonding, composite resin penetrates into the enamel as a result of acid etching. The depth of penetration depends on the acid used, the etching pattern and prism direction, something not homogeneous on all teeth (Øgaard et al., 2004). Alterations can be observed microscopically of up to 100 to 200 µm (Legler et al., 1990; Zentner and Duschner, 1996).

Regarding debonding, the most significant adverse effects that may occur are the following: fractures (Eliades et al. 1993), loss of the fluoride-rich uppermost enamel layer (more than 10µm) (Mizrahi, 1982) and an increase in roughness after resin grinding (Eliades et al., 2004). Additionally, the clinician may also encounter enamel cracks after the removal of fixed appliances. Their prevalence has been reported to be as high as 50% with vertical cracks, which are highly correlated with debonding forces, being the most common. In the unfortunate case of the occurrence of a large number of horizontal cracks after debonding, these are most probably due to improper bonding/debonding techniques (Bishara and Dale, 1997). However, an interesting finding regarding this clinical aspect is that the teeth having pre-existing pronounced enamel micro-cracks at the beginning of treatment do not present greater increase in micro-cracks after debonding of metallic brackets or ceramic brackets, followed by residual adhesive removal (Dumbryte et al., 2013).

As far as enamel color alterations are concerned, chemically cured resin has been reported to induce greater color changes than light-cured composite. However, overall, the color of teeth is changed after orthodontic treatment by means of fixed appliances (Karamouzos et al., 2010).

Decalcification and enamel surface loss may be observed during the course of orthodontic treatment. Decalcification in the form of white spot lesions is the most important iatrogenic effect of fixed appliance orthodontic treatment (Gorelick et al., 1982). It is only to be expected that the maintenance of a good oral hygiene is more difficult for orthodontic patients than for individuals without appliances, and a rapid increase in the volume of dental plaque with a lower resting pH than in non-orthodontic subjects is to be anticipated during treatment with fixed appliances (Gwinnett and Ceen, 1979). The mandibular first molars and maxillary lateral incisors are usually the teeth most affected (Lucchese and Gherlone, 2013). Significant decalcification may be observed six months after orthodontic bonding. This is the reason why early diagnosis is of critical importance (Lucchese and Gherlone, 2013).

2.2. Tooth wear

Occlusal wear is defined as "the loss of substance on opposing occlusal units or surfaces as the result of attrition or abrasion" (Glossary of Prosthodontic Terms, 2017).

The processes that the literature has reported as associated with tooth wear are attrition, abrasion, erosion or combinations. More specifically, "attrition is mechanical wear occurring as a consequence of mastication or parafunction and is located on the contacting surfaces of the teeth" (Glossary of Prosthodontic Terms, 2017). On the other hand, "abrasion is known to be the abnormal wearing away of the tooth substance by causes other than mastication, usually a foreign element" (Glossary of Prosthodontic Terms, 2017). Last but not least, erosion has been defined as "the gradual loss of tooth substance by means of chemical processes without the involvement of bacterial action" (Glossary of Prosthodontic Terms, 2017).

Several parameters have been correlated with tooth wear in the general population. It has been well established from the results of various epidemiological studies that the occurrence of tooth surface loss increases with age (Egermark-Eriksson et al., 1987; Ritchard et al., 1992; Johansson et al., 1993; Johansson et al., 1993; Silness et al., 1993; Shaw, 1997; Casanova-Rosado et al., 2005; Van't Spijker et al., 2009; Cunha-Cruz et al., 2010) and that the history of tooth wear in childhood is related to the development of tooth wear in adulthood (Knight et al., 1997). In regards to gender, most studies have suggested that men exhibit increased wear compared to women (Johansson et al., 1993; Johansson et al., 1993; Mwangi et al., 2009; Van't Spijker et al., 2009; Cunha-Cruz et al., 2010). As far as the number of missing teeth is concerned, partially edentulous patients have been shown to have more severe wear (Bernhardt et al, 2004; Wazani et al., 2012; Zhang et al, 2014), although this association is not always clinically significant (Smith and Robb, 1996; Zhang et al., 2014). In addition, it has been claimed that underlying systemic predisposing factors and dietary habits such as alcohol, sour fruit, carbonated drink intake and acidic products in general may also make some contribution to tooth wear (Chuajedong et al, 2002; Bartlett et al, 2011; Okunseri et al., 2015; Wei et al, 2016). Finally, socioeconomic and environmental adversities also seem to play some role in the development of tooth wear (Zhang et al, 2014; Okunseri et al., 2015; Wei et al, 2016).

2.2.1. Wear of teeth and occlusion

Among the parameters that have been claimed to contribute to, or to decrease occlusal wear, are various adverse occlusal conditions. Bernhard et al. (2004) found that edge-to-edge or cusp-to-cusp relationships or loss of natural occlusal support zones may cause high occlusal wear. In contrast, the existence of crowding and crossbite may prevent high wear by offering stability in the interocclusal contact pattern (Bernhardt et al., 2004). Other occlusal situations that have been considered predictors of wear in maxillary and mandibular incisors are increased overbite and overjet (Silness et al., 1993). Although there is agreement about overbite, Ritchard et al. (1992) argued that a patient' s attrition score has a tendency to decrease initially with overjet until a critical value, and then increases.

Moreover, patients who exhibit a forced bite and a Class II, division 2 malocclusion have been shown to demonstrate a higher prevalence of dental wear (Grzegocka et al., 2016). Earlier studies had already identified an association of Class II malocclusion with tooth wear, without, however, specifying the division (Casanova-Rosado et al., 2005; Cunha-Cruz et al., 2010). As far as Class II divisions are concerned, two studies have been conducted with the aim of comparing tooth wear patterns between normal occlusion and Class II, division 1 and Class II, division 2 malocclusions, respectively (Janson et al., 2010; Oltramari-Navarro et al., 2010). Both studies concluded that the difference in tooth wear patterns is the consequence of the differences in interocclusal tooth arrangement.

2.2.2. Wear of teeth, muscle function and craniofacial morphology

Muscle function and craniofacial morphology have long been considered to be interrelated in the orthodontic literature (Kaklamanos et al., 2002). Subjects with a strong bite force exhibit a more anteriorly inclined mandible, a smaller anterior and greater posterior facial height in contrast to those with weak bite force who displayed a longer anterior and shorter posterior facial height, and a larger gonial angle (Ringqvist, 1973; Ingervall and Helkimo, 1978; Proffit et al., 1983; Weijs et al., 1984; Van Spronsen et al., 1991; Kiliaridis and Kalebo, 1991). Corroborating evidence has shown that adults suffering from myotonic dystrophy were found to have weak masticatory muscles, exhibited an increased prevalence of Angle's

Class II malocclusion, anterior open bite, posterior crossbite, as well as an open bite skeletal pattern with a vertical excess of the lower anterior facial height (Kiliaridis et al., 1989).

Not surprisingly, an individual's ability to produce high levels of bite force has also been correlated with increased occlusal wear (Ingervall and Helkimo, 1978; Helkimo and Ingervall, 1978; Waltimo et al., 1994; Kiliaridis et al., 1995). Despite the fact that these findings are not universally accepted (Dahl et al., 1985), it seems that a possible explanation of the relation between tooth wear and the development of a specific craniofacial morphology is the common influence of muscle activity. Although it has been reported that both bruxers who are subjects with high scores of tooth wear, as well as, non-bruxers exhibit similar facial types (Menapace et al. 1994), other studies have identified a statistically significant difference in their bizygomatic and cranial widths (Young et al., 1999). It is also interesting to note that research findings demonstrate a small but significant relationship between craniofacial morphology during childhood and tooth wear in adulthood (Almond et al., 1999).

2.2.3. Wear of teeth during orthodontic treatment

Although, pronounced wear is not to be expected over a relatively short period, such as the course of orthodontic treatment (Panos et al., 2011), up to now only limited data seem to be available regarding tooth surface loss over and above the physiological alterations to the dentition (Øgaard et al., 2004). Specific reference has been made to the possibility that ceramic brackets induce excessive tooth wear when they come into contact with the opposing teeth (Douglass, 1989; Viazis et al., 1990; Bishara and Dale, 1997).

3. AIM

3.1. Aim of the systematic review

To investigate current data on tooth wear in patients having undergone orthodontic treatment and critically evaluate the quality of available evidence.

3.2. Objectives of the systematic review

To retrieve data on volumetric and surface tooth wear measurements of patients before and after orthodontic therapy.

3.3. Null hypothesis

There is no difference in volumetric and surface tooth wear of patients before and after orthodontic treatment.

4. MATERIALS AND METHODS

4.1 Protocol development and registration

The present review was based on a specific protocol developed and piloted following the guidelines outlined in the PRISMA-P statement (Shamseer et al., 2015) and registered in PROSPERO (CRD42017078206). In addition, conduct and reporting followed the Cochrane Handbook for Systematic Reviews of Interventions (Higgins and Green, 2011) and the PRISMA statement (Moher et al., 2009), respectively.

4.2. Eligibility criteria

The selection criteria for the domains of study design, participants' characteristics, intervention characteristics and principal outcome measures applied for the present review were as follows:

4.2.1. Types of study design

Studies that were included had to be observational studies evaluating tooth wear immediately before and after the completion of comprehensive orthodontic treatment. Animal studies and reviews (traditional reviews, systematic reviews and meta-analyses) were not included in the present investigation.

The type of study design was assessed using the algorithm available from SIGN (Scottish Intercollegiate Guidelines Network) available from http://www.sign.ac.uk (Appendix II).

4.2.2. Types of participants

The included studies could involve patients of any age and gender. Studies that included patients with clefts, syndromes or congenital anomalies of the craniofacial region, congenitally missing teeth, developmental dental anomalies, parafunctional habits or temporomandibular disorders were excluded.

4.2.3. Types of interventions

The included studies could involve patients who received comprehensive orthodontic treatment of any type. However, interventions including orthognathic surgery were excluded.

4.2.4. Types of outcome measures

The studies included in the present review had to provide measurements on tooth wear which were either volumetric tooth substance loss or surface tooth wear using grading scales.

4.3. Information sources and search strategy

The principal investigator (MAM) developed detailed search strategies for each database. These were based on the strategy developed for MEDLINE, but revised appropriately for each database to take account of the differences in controlled vocabulary and syntax rules. The following electronic databases were searched (Appendix III): MEDLINE via PubMed, CENTRAL, Cochrane Systematic Reviews, Scopus, Web of Science™ Core Collection, Arab World Research Source, Clinical Trials registry and ProQuest Dissertations & Theses Global database.

No restriction was placed on the language, date or status of publication. In addition, efforts were made to obtain conference proceedings and abstracts where possible and the reference lists of all eligible studies for additional records were searched.

4.4. Study selection

The principal investigator (MAM) and the thesis co-supervisor (EGK) assessed the retrieved records for inclusion independently. They were not blinded to the identity of the authors, their institution, or the results of the research. They obtained and assessed, again independently, the full report of records considered by either reviewer to meet the inclusion criteria. Disagreements were resolved by discussion or consultation with the principal supervisor (AEA). All decisions on study identification were recorded.

4.5. Data collection and data items

The same two persons (MAM and EGK) performed data extraction independently and any disagreements were again resolved by discussion or consultation with the thesis principal supervisor (AEA). Data collection forms were used to record the desired information.

a. Bibliographic details of the study.

b. Details on study design and verification of study eligibility.

c. Participant characteristics (where available number, age, gender).

d. Intervention characteristics (e.g. kind of appliances, orthodontic treatment with/without extractions).

e. Details on outcomes assessed and assessment procedures.

f. Additional information: a prior sample size calculation, methodology reliability assessment.

If clarifications were needed regarding the published data, or additional material was required, then attempts to contact the corresponding authors would be made.

The outcomes relevant to occlusal wear after orthodontic treatment retrieved from the studies included in the present review were categorized as follows:

a. Surface tooth wear measurements using grading scales.

b. Volumetric tooth wear measurements.

4.6. Risk of bias in individual studies

The principal investigator (MAM) and the thesis co-supervisor (EGK) assessed the risk of bias in the included studies, independently and in duplicate, during the data extraction process, using the ROBINS-I tool (Risk Of Bias In Non-randomised Studies of Interventions) (Sterne et al., 2016). Any disagreements were resolved by discussion or consultation with the thesis principal supervisor (AEA). The ROBINS-I tool assessment tool includes the following domains:

a. Bias due to confounding.

b. Bias in selection of participants into the study.

c. Bias in classification of interventions.

d. Bias due to deviations from intended interventions.

e. Bias due to missing data.

f. Bias in measurements of outcomes.

g. Bias in selection of the reported results.

After entering in the data extraction form the information reported in each study, every domain would receive a judgment of either low, moderate, serious or critical risk of bias or the label "no information" (indicating no information on which to base a judgment about risk of bias for this domain) (Sterne et al., 2016).

Subsequently, studies were to be judged as being of low, moderate, serious or critical risk of bias (Sterne et al., 2016):

a. Low risk of bias: The study is comparable to a well performed randomized control.

b. Moderate risk of bias: The study provides sound evidence for a non-randomized study but cannot be considered to be a well performed randomized trial.

c. Serious risk of bias: The study has some important problems.

d. Critical risk of bias: The study is too problematic to provide any useful evidence and should not be included in any synthesis.

e. No information: There is no information on which to base a judgment about risk of bias.

4.7. Summary measures and synthesis of results

In situations where the retrieved data used different variables measuring the same concept on different scales with a high degree of correlation, the effects of the interventions were planned to be expressed as standardized values (i.e. the Standardized Mean Difference (SMD) together with the relevant 95% Confidence Interval (CI)), in order to enable quantitative synthesis (Deeks et al., 2001). In cases where a particular comparison of the same variable was recorded, the intervention effect was planned to be expressed as the Weighted Mean Difference (WMD) together with the 95% CI.

The random effects method for meta-analysis was to be used to combine data from studies that reported similar measurements in appropriate statistical forms (Der Simonian and Laird, 1986, Borenstein et al., 2009), since they were expected to differ across studies due to clinical diversity in terms of participant and intervention characteristics.

To identify the presence and extent of between-study heterogeneity, the overlap of 95% CI for the results of individual studies was to be inspected graphically, and Cochrane's test for homogeneity and the I^2 statistic were to be calculated (Higgins and Green, 2011). The results of the I^2 statistic were to be interpreted as follows (Higgins and Greene, 2011):

- I^2 from 0% to 40%: heterogeneity might not be important;
- I^2 from 30% to 60%: may represent moderate heterogeneity;
- I^2 from 50% to 90%: may represent substantial heterogeneity;
- I^2 from 75% to 100%: considerable heterogeneity.

All analyses were to be carried out with Comprehensive Meta-analysis software 2.2.046 (©2007 Biostat Inc., New Jersey, USA). Significance (a) was set at 0.05, except for 0.10 used for the heterogeneity tests (Ioannidis, 2008).

4.8. Risk of bias across studies and additional analyses

If a sufficient number of trials were identified, analyses were planned for "small-study effects" and publication bias (Higgins and Green, 2011). If deemed possible, exploratory subgroup analyses were planned according to participant and intervention characteristics. Finally, the quality of evidence was assessed based on the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach (Guyatt et al., 2011).

5. RESULTS

5.1. Study selection

The flowchart of records through the reviewing process is shown in Figure 1. The data search took place on October 1st, 2017. Initially 4389 records were identified, 1728 were identified as duplicates, a further 2657 were excluded on the basis of their title and abstract, and one because tooth wear had not been assessed immediately before and after orthodontic treatment. Finally, three full-text reports were included in the systematic review (Kuijpers et al., 2009; Panos et al., 2011; Park et al., 2014).

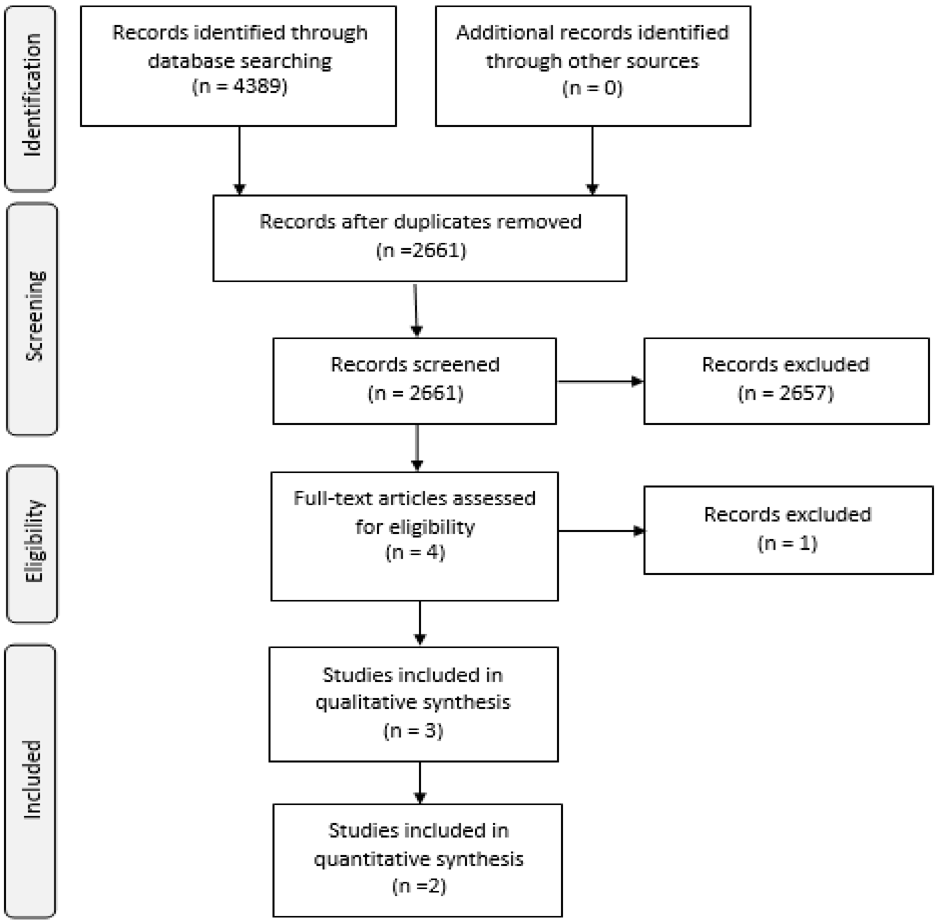

Figure 1. Flowchart of records through the reviewing process.

5.2. Study characteristics

The general characteristics of the studies included in the present systematic review, as well as sample characteristics, are presented in Tables 1 and 2. They were published between 2009 and 2014 and investigated either surface tooth wear using grading scales on the upper and lower anterior teeth (Kuijpers et al., 2009) or measured the differences in tooth volume before and after comprehensive orthodontic treatment (Panos et al., 2011; Park et al., 2014). The length of the orthodontic treatment varied on average from 29 to 35.5 months. Although Kuijpers et al. (2009) did not mention details of the treatment modalities of their sample, Panos and co-workers (2011) selected patients who had undergone orthodontic treatment by means of stainless steel brackets and bands, either without extractions or accompanied by two maxillary or four premolar extractions. On the other hand, Park et al. (2014) investigated patients who had received orthodontic treatment with four premolar extractions but without providing any further information about the type of brackets and bands used. With regard to age, Kuijpers et al. (2009) and Park et al. (2014) selected patients less than 15 years old, and adults, respectively while Panos et al. (2011) studied adolescents as well as young adults. Other variables, apart from the assessment of occlusal wear, that were considered in these studies were Little’s Irregularity Index, intercanine width, duration of treatment, gender, age, performance of extractions or not, type of teeth, type of initial malocclusion, ANB angle and Frankfort-mandibular angle.

Table 1. General characteristics of the studies included in the systematic review.

Study	Intervention characteristics	Teeth assessed and assessment methods	Other variables	Additional information
Kuijpers et al., 2009	Comprehensive orthodontic treatment. [bracket type not mentioned]	**Incisors [U & L]:** Silness et al (1993) grading scale **Canines [U & L]:** grading scale adapted from Carlsson et al. (1985) & Bauer et al. (1997)	Little's Irregularity Index, intercanine width	Power calculations: No Method error: kappa statistics
Panos et al., 2011	Comprehensive orthodontic treatment without extractions or accompanied with 2 maxillary or 4 premolar extractions. [stainless steel brackets]	**Incisors, Canines, Premolars & molars [U & L]:** 3D volumetric measurements [3D CT scan]	Tx duration, gender, extractions or not, type of tooth, type of malocclusion	Power calculations: No Method error: Dahlberg's formula
Park et al., 2014	Comprehensive orthodontic treatment with 4 premolar extractions. [bracket type not mentioned]	**Canines [U & L]:** 3D volumetric measurements [laser scanning]	Gender, age, Tx duration, ANB angle, FMA angle	Power calculations: No Method error: Dahlberg's formula

FMA: Frankfort-Mandibular plane angle, L: lower, U: upper, Tx: treatment

Table 2. Sample characteristics in the studies included in the systematic review.

Study	Inclusion & exclusion criteria	Analyzed sample
Kuijpers et al., 2009	**Inclusion criteria:** maximum 15 years of age at the start; treatment with full fixed appliances; dental casts available at three time-points until 5 years post-treatment **Exclusion criteria:** clefts or craniofacial anomalies; anomalies or absence of any of the incisors; developmental dental malformations; combined orthodontic-surgical or orthodontic-periodontal cases; damaged or broken incisors; prosthetic replacements or crowns	222 patients (80 M, 142 F): pre- & post-treatment casts Age at the beginning of Tx: 11.65 ±1.30 years [range: 8.04-15] Age at the end of Tx: 14.49 ±1.42 years [range: 11.08-19.2]
Panos et al., 2011	**Inclusion criteria:** Patients without any specific health problems; all permanent teeth had to have erupted; all dental casts had to be of high quality **Exclusion criteria:** High-risk patients with parafunctional habits, occupational hazards or unusual dietary habits; patients with fractured teeth and temporomandibular disorders; individual teeth with their crown restored during orthodontic treatment	30 patients (15 M, 15F): pre- & post-treatment digitized casts 628 teeth: 194 incisors; 118 canines; 316 premolars & molars Age at the beginning of Tx: 14.4 [range: 11-24.5] Malocclusion type: 10 Class I; 15 Class II/1; 4 Class II/2; 1 Class III Treatment protocol: 8 2 Mx Pm extractions; 2 4 Pm extractions; 20 non-extraction Tx duration: 29 months [range: 24-52]; 12 patients> 30 months; 18 patients<30 months
Park et al., 2014	**Inclusion criteria:** Complete permanent dentition; $0^o<ANB<4^o$; normal vertical pattern; absence of anterior crossbite **Exclusion criteria:** restorations of the anterior teeth; occlusal adjustments during orthodontic treatment	56 patients (23 M, 33 F): pre- & post-treatment digitized casts 224 canines Age at the beginning of Tx: 21.8 ±5.1 years Tx duration: 35.5 ±8.3 months

M: males: F: females; Tx: treatment; Mx: Maxillary; Pm: premolars

5.3. Risk of bias within studies

Table 3 presents the summary of findings regarding risk of bias assessment for the three included studies (Kuijpers et al., 2009; Panos et al., 2011; Park et al., 2014). All of these were considered overall as being of serious risk of bias.

In general, all studies included in the present review were considered to present serious risk of bias regarding confounding, as important parameters (like the natural progression of tooth wear with age, gender, malocclusion type, craniofacial morphology, treatment duration, etc.) were not always appropriately controlled. In contrast, the risk of bias in the selection of participants and classification of interventions were found to be low. The risk of bias in the measurement of outcomes was considered low for two studies (Panos et al., 2009; Park et al., 2011) but moderate for the Kuijpers and co-workers (2009) study, as inherent limitations exist in the procedure of standardization and reliability of assessing wear of teeth using grading scales. Finally, the risk of bias in selection of the reported result was deemed to be moderate.

Table 3. Summary of the risk of bias assessment.

Domain	Kuijpers et al., 2009	Panos et al., 2011	Park et al., 2014
Bias due to confounding	Serious	Serious	Serious
Bias in selection of participants for the study	Low	Low	Low
Bias in classification of interventions	Low	Low	Low
Bias in measurement of outcomes	Moderate	Low	Low
Bias in selection of the reported result	Moderate	Moderate	Moderate
Overall	Serious	Serious	Serious

5.4. Results of individual studies and synthesis of results

The results of the studies included in the present review are presented below.

5.4.1. Surface tooth wear measurements using grading scales

The only study that investigated surface tooth wear using grading scales on the upper and lower incisors and canines observed an increase in wear for all examined teeth over a mean of 2.8 years of treatment duration (Kuijpers et al., 2009). [Incisors: Pre-Tx (Mean ±SD): 1.18 ±0.54, Post-Tx: 2.0 ±0.57, $p<0.001$; Canines: Pre-Tx: 0.42 ±0.54, Post-Tx: 1.52 ±0.60, $p<0.001$]. No gender difference was noted, as well as, associations with Little's Irregularity Index.

5.4.2. Volumetric tooth wear measurements

The two studies that measured the volume of lost tooth substance during orthodontic treatment on digitized casts by means of 3D volumetric measurements (Panos et al., 2011; Park et al., 2014) also reported tooth substance loss. The mean volume reduction was 1.02 mm^3 for the incisors [95% Confidence Interval (CI): 0.84 – 1.20; 1 study, n = 30 participants and 194 teeth] (Panos et al., 2011), 1.62 mm^3 for the canines [95% CI: 0.87 – 2.38; 2 studies, n = 86 participants and 342 teeth; I^2 = 96 %] (Panos et al., 2011; Park et al., 2014) and 0.95 mm^3 for premolars and molars [95% CI: 0.84 – 1.07; 1 study, n = 30 participants and 316 teeth] (Panos et al., 2011). The mean treatment durations for the Panos et al. (2011) and Park et al. (2014)

studies were 29 months (with a range of 24 to 52 months) and 35.5 ±8.3 months, respectively.

Panos and co-workers (2011) did not observe significant differences between gender, extraction / non extraction treatment, and different malocclusion classifications. Similarly, Park et al. (2014) did not report statistically significant correlations between tooth wear and gender, treatment duration and ANB and Frankfort-mandibular plane angles.

5.5. Risk of bias across studies and additional analyses

Because it was not possible to retrieve a sufficient number of trials, we were not able to conduct analyses for "small-study effects" and publication bias (Higgins and Green, 2011). Overall, the quality of evidence was considered as low (Table 4).

Table 4. Quality of available evidence.

Quality assessment						Teeth	Effect	Quality
Studies	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**		**Absolute Mean (95% CI)**	
Surface tooth wear | Incisors[assessed with Silness et al. (1993) grading scale]								
1	Serious[1]	Not serious	Not serious	Serious[2]	No	888	Mean **0.82 grades higher** ***p*<0.001**	⊕⊕◯◯ **LOW**
Surface tooth wear | Canines[assessed with grading scale adapted from Carlsson et al. (1985) and Bauer et al. (1997)]								
1	Serious[1]	Not serious	Not serious	Serious[2]	No	848	Mean **1.10 grades higher** ***p*<0.001**	⊕⊕◯◯ **LOW**
Volumetric tooth substance loss | Incisors [assessed in mm³]								
1	Serious[1]	Not serious	Not serious	Serious[2]	No	194	Mean **1.02 mm³ higher** (0.84 higher to 1.20 higher) ***p*=0.000**	⊕⊕◯◯ **LOW**
Volumetric tooth substance loss | Canines [assessed in mm³]								
2	Serious[1]	Not serious	Not serious	Serious[3]	No	342	Mean **1.62 mm³ higher** (0.87 higher to 2.38 higher) ***p*=0.000**	⊕⊕◯◯ **LOW**
Volumetric tooth substance loss | Premolars & molars [assessed in mm³]								
1	Serious[1]	Not serious	Not serious	Serious[2]	No	316	Mean **0.95 mm³ higher** (0.84 higher to 1.07 higher) ***p*=0.000**	⊕⊕◯◯ **LOW**

CI: Confidence interval
[1] Studies were considered as being of serious risk of bias. [2] The results are based only on one study. [3]The results are based only on two studies.

6. DISCUSSION

6.1. Summary of evidence

It has been suggested that loss of tooth substance due to wear additional to the expected changes may occur during comprehensive orthodontic treatment (Dahl et al., 1985, Øgaard et al., 2004). Based on the information provided in the present review, the degree of tooth wear during treatment with metallic fixed appliances may vary. However, the concerns raised during quality assessment of the available evidence provide insights regarding the confidence in the observed estimates.

Although pronounced wear during a relatively short period, such as the course of orthodontic treatment, is not to be expected (Panos et al., 2011), the only study that investigated surface tooth wear in 222 patients, using grading scales on the upper and lower incisors and canines, observed an increase in wear for all examined teeth (Kuijpers et al., 2009). In general, the canines showed the most severe progression of wear in terms of difference before and after treatment, although the incisors exhibited greater absolute measurements post treatment. The aim of this survey was not to examine whether the amount of anterior tooth wear differed between orthodontic and non-orthodontic subjects as it did not include observation of an untreated control group (Kuijpers et al., 2009). Previous investigations in non-patient subjects showed similar patterns of wear of permanent anterior teeth in children, adolescents and young adults under observation for similar periods of time (Könönen et al., 2006; Silness et al., 1997), although the changes were not statistically significant for all teeth (Silness et al., 1995).

The other two included studies (Panos et al., 2011; Park et al., 2014) that involved 86 patients in total and measured the volume of lost tooth substance during orthodontic treatment on digitized casts, also reported mean volume decreases. Once again, the absence of control groups did not permit investigating whether the reduction is associated with orthodontic treatment, physiologic alterations of the dentition or a combination of both factors on answering the question whether orthodontic wear constitutes a pathological condition or not (Bartlett and Dugmore, 2008). Pintado and co-workers (1997) followed young untreated healthy adults over a 2 year period and observed a mean tooth volume loss of 0.098 ± 0.331 mm^3 (canines: 0.173 ± 0.530 mm^3; premolars: 0.047 ± 0.063 mm^3; molars: 0.063 ± 0.096 mm^3), which is significantly smaller than the decreases reported in the present review. In addition to the reported mean values of tooth wear, the accompanying high standard deviations are indicative of the extent of the biologic variation involved in the related phenomena (Panos et al., 2011; Pintado et al., 1997).

As tooth surface loss increases with age (Könönen et al., 2006; Silness et al., 1997; Pintado et al., 1997), it is also important to consider duration of the treatment over which the aforementioned changes were observed. In the survey of Kuijpers et al. (2009), patients were treated over a mean period of 2.8 years, whereas mean treatment duration for the Park et al. (2014) study was 35.5 ±8.3 months. The latter investigators did not observe any statistically significant correlation between tooth wear and treatment length. However, Panos et al. (2011) demonstrated a statistically significant increase in the mean tooth volume reduction in the group of patients treated for 30 or more months compared to those where the treatment did not exceed this threshold, suggesting that treatment should be as short as possible. Finally, when considering the parameter of time in relation to tooth surface loss, it should be noted that the included studies and the age groups of the patients were not completely comparable. Kuijpers et al. (2009) and Park et al. (2014) investigated patients less than 15 years old, and adults, respectively. In contrast, the Panos et al. (2011) study involved both adolescents and young adults.

Apart from the tendency towards increasing tooth surface loss with age (Könönen et al., 2006; Silness et al., 1997; Pintado et al., 1997), variations in wear of teeth have also been associated with other parameters. Gender differences have been suggested in both adolescents and adults (Dugmore and Rock, 2004; Bardsley et al., 2004; Van't Spijker et al., 2009). Based on the retrieved data, no statistically significant differences were identified (Panos et al. 2011; Park et al. 2014), while Kuijpers and co-workers (2009) did not make any comparisons between males and females. Moreover, underlying systemic predisposing factors, dietary habits and socio-economic parameters have also been suggested as influencing the degree of tooth wear in children and adolescents (Milosevic et al., 2004; Sanhouri et al., 2010; Wang et al., 2010; Mantonanaki et al., 2013; Hamasha et al., 2014). Among the included studies, Panos et al. (2011) excluded from further consideration subjects with parafunctional habits, occupational hazards and unusual dietary habits, whereas Kuijpers and co-workers (2009) excluded from their study models showing signs of extensive wear, wear of cusps and cupping of the occlusal surfaces of molars already existing before treatment in an attempt to control the influence of dietary habits or bruxism.

Craniofacial morphology and malocclusion have also been associated with the wear of teeth (Almond et al., 1999; Bernhardt et al., 2004; Ritchard et al., 1992; Silness et al., 1993; Casanova-Rosado et al., 2005; Cunha-Cruz et al., 2010; Grzegocka et al., 2016). Park et al. (2014) did not observe statistically significant correlations between tooth wear and ANB or Frankfort-mandibular plane angles in the group of subjects studied that exhibited skeletal Class I and normal vertical pattern. The measurements by Panos et al. (2011) did not reach statistical significance when mean volume reductions in patients with Class I, Class II, division 1 and Class II, division 2 malocclusions were compared, while Kuijpers and co-workers (2009) observed no association between the degree of Irregularity Index and the amount of anterior tooth wear, contrary to investigations in subjects not subjected to orthodontic treatment (Berge et al., 1996).

In terms of orthodontic treatment characteristics, the decision of whether to extract permanent teeth, or not, has also been suggested to have an impact on the development of occlusal wear, due to the development of more premature contacts during the usually larger tooth movements involved (Panos et al., 2011). Kuijpers et al. (2009) did not report any relevant information, while Park et al. (2014) included only four premolar extraction cases. Panos et al. (2011), who made comparisons between extraction and non-extraction cases, observed an increase in occlusal wear in the former group, that, however, did not reach statistical significance. Moreover, an increase in the upper intercanine width during treatment was associated with less increase in wear (Kuijpers et al. 2009).

Overall, the quality of evidence included in the retrieved studies, based on the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach (Guyatt et al., 2011), was considered as low. Apart from concerns regarding the precision of the observed estimates, in general, all studies were considered to present serious risk of bias, as confounding parameters were not always appropriately controlled for. The risk of bias in the measurement of outcomes was considered moderate for the Kuijpers et al. (2009) study, as measurement of tooth wear with the use of grading scales is considered controversial (Bardsley, 2008). It has been reported that these methods are not suitable for the identification of the progression of the relative minor wear that is likely to occur during the course of treatment with fixed orthodontic appliances (Park et al., 2014), because of the limitations inherent in the procedure of standardization and measurement reliability (Al-Omiri et al., 2010; Lobbezoo and Naeije, 2001). The investigators in the study of Kuijpers et al. (2009) reported difficulties in validating incisor wear measurement with the scale employed and moderate to substantial Kappa values for intra-observer reliability, despite calibration and training. For the other two studies (Panos et al., 2009; Park et al., 2011) the risk of bias was considered low and the method's error was reported to be 0.19 mm^3 and 0.20 mm^3 respectively. However, all three studies could potentially suffer from problems associated with the procedures of debonding and taking impressions with alginates. It has been reported that, after the removal of fixed appliances, there may be as much as 2.48 ± 0.92 mm^3 of resin remnants and 0.05 ± 0.26 mm^3 of enamel loss following polishing procedures (Ryf et al., 2012). In another relevant study that investigated the quantity of adhesive remnants and enamel loss after debonding of molar tubes, the results showed that the maximum height of adhesive remaining on enamel surface was 0.76 mm and the volume on particular teeth ranged from 0.047 mm^3 to 4.16 mm^3. Mean depth of enamel loss for particular teeth ranged from 0.0076 mm to 0.0416 mm (Janiszewska-Olszowska et al., 2014). Shrinking of the alginate or expansion of gypsum during setting could induce an additional variation in the results, as well (Park et al., 2014).

6.2. Strengths and limitations

The strengths of the present review include using a methodology following well-established guidelines. To our knowledge, there has been no other systematic review conducted on volumetric and surface tooth wear in patients having undergone orthodontic treatment.

Moreover, the search strategy employed in the present review was both exhaustive, covering electronic, manual, and gray literature material up to October 2017, and comprehensive including every available study investigating the impact of orthodontic treatment on tooth wear, irrespective of language, date and status of publication. Every effort to decrease bias in the methodology employed was made. Screening, verification of eligibility, abstraction of information, assessment of risk of bias and of the quality of evidence were all performed in duplicate, and any disagreement was resolved by discussion or consultation until a final consensus was achieved. Finally, the random effects model was employed during exploratory quantitative data synthesis to incorporate any observed heterogeneity (Lau et al., 1997).

There are also some limitations to the present review, arising mainly from the nature and the characteristics of the data retrieved during the review process, which resulted in the assessment of the level of available evidence as low. The scarcity of relevant information lead to meta-analytic procedures that attempted to be regarded as only exploratory until additional research becomes available. However, current concepts support that even data from as few as two studies can be combined, provided that these can be meaningfully pooled (Ryan, 2013), as all other summarizing techniques are less transparent and/or are less likely to be valid (Valentine et al., 2010). Furthermore, exploratory subgroup analyses and analyses for "small-study effects" and publication bias (Higgins and Green, 2011), could not be carried out even though they were incorporated as possibilities according to the review protocol. Moreover, in some cases the small number of patients finally analyzed resulted in subsequent problems regarding the precision of the effect estimates.

Another limitation of the data retrieved in this study stems from the absence of control groups where no intervention took place. Although there is information about the varying degrees of tooth surface loss after comprehensive orthodontic treatment, the lack of controls precludes assumption on the proportion of the reduction associated with orthodontic treatment or due to physiologic alterations of the dentition.

In addition, varying confounding parameters were not always appropriately controlled for, and the investigations did not cover the whole extent of the dentition. Only Panos et al. (2011) made measurement for all tooth categories (incisors, canines, premolars and molars), whereas Park et al. (2014) studied only canines, and Kuijpers et al. (2009) investigated the tooth wear only on incisors and canines.

In addition, limitations may arise from pooling in the retrieved studies of the results from different teeth in the same outcome, without relevant statistical adjustments. Meta-analysis of these studies would ideally require knowledge of a measure of the correlation of the data (Smaïl-Faugeron et al., 2014). Such a measure was not reported, and would have warranted the retrieval of the entire data set for each trial. However, this was not attempted. It has also to be acknowledged that the results of this review may relate mostly to patients treated with metallic brackets.

6.3. Recommendations for future research

Although pronounced wear over a relatively short period, such as the course of orthodontic treatment, is not to be expected (Panos et al., 2011), the data included in the present review showed that varying degrees of tooth surface loss may occur after comprehensive orthodontic treatment. In order to investigate the phenomenon more comprehensively and elucidate the effects during orthodontic treatment additional to the physiologic alterations of the dentition, further research is warranted.

It has been suggested that well-designed and properly executed Randomized Control Trials provide the best evidence, with a decreased risk of bias on the efficacy of health care interventions (Altman et al., 2001; Oxford Centre for Evidence-based Medicine, 2009). Since, this might be unethical under certain situations, the random allocation of subjects either to a group where they would receive orthodontic treatment or to a group of no intervention, it would be advisable to conduct at least well-controlled prospective non-randomized studies that are comparable to well-performed randomized studies (Sterne et al., 2016). Particular importance should be placed on possible ways to control bias due to confounding and bias in measurement of outcomes. Finally, since special reference has been made to the possibility that ceramic brackets induce excessive tooth wear when they come into contact with the opposing teeth (Douglass, 1989; Viazis et al., 1990; Bishara and Dale, 1997), future studies should investigate tooth surface loss in such cases in addition to subjects treated with the more recent aligner techniques.

7. CONCLUSIONS

Varying degrees of tooth surface loss were found to occur after comprehensive orthodontic treatment. Further studies are needed in order to elucidate how much of the reduction is directly associated with orthodontic treatment and how much is due to physiologic alterations of the dentition.

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Appendix I. Systematic review protocol used for registration with international prospective register of systematic reviews (PROSPERO).

Review question(s)

To investigate current data on tooth wear in patients with malocclusion.

Searches

Comprehensive electronic database searches will be undertaken without language restriction in the following databases: MEDLINE via PubMed (http://www.ncbi.nlm.nih.gov/pubmed), Scopus (www.scopus.com), Web of Science™ Core Collection (http://apps.webofknowledge.com/), Arab World Research Source (http://0-web.a.ebscohost.com.amclb.iii.com) and ProQuest Dissertations & Theses Global database. Efforts will be made to obtain conference proceedings and abstracts where possible. Authors will be contacted to identify unpublished or ongoing clinical trials and to clarify methodology and data as necessary. Reference lists of included studies will be screened for additional relevant research.

Types of study to be included

The trials to be included should be observational studies evaluating tooth wear in patients with malocclusion, or immediately before and after the completion of comprehensive orthodontic treatment.

Condition or domain being studied

Tooth wear in patients with malocclusion

Participants/ population

Subjects of any age and gender.

Intervention(s), exposure(s)

Patients with malocclusion. Patients having received comprehensive orthodontic treatment of any type. However, interventions including orthognathic surgery were excluded.

Comparator(s)/ control

No treatment (if applicable).

Outcome(s)

Primary outcomes

Measurements on tooth wear either volumetric tooth substance loss or surface tooth wear using grading scales.

Secondary outcomes

None.

Risk of bias (quality) assessment

Assessment of risk of bias will be performed independently and in duplicate by two investigators (MAM and EGK) using the using the ROBINS-I tool (Risk Of Bias In Non-randomised Studies of Interventions). Disagreements will be resolved by discussion and consultation with a third author where necessary (AEA).

Strategy for data synthesis

In situations where the retrieved data use different variables measuring the same concept on different scales with a high degree of correlation, the effects of the interventions are planned to be expressed as standardized values (i.e. the

Standardized Mean Difference (SMD) together with the relevant 95% Confidence Interval (CI)), in order to enable quantitative synthesis. In case that in a particular comparison the same variable is recorded, the intervention effect is planned to be expressed as the Weighted Mean Difference (WMD) together with the 95% CI. The random effects method for meta-analysis is to be used to combine data from studies that report similar measurements in appropriate statistical forms, since they are expected to differ across studies due to clinical diversity, in terms of participant and intervention characteristics. Heterogeneity will be assessed using both the Chi-squared test and the I-squared statistic. If an adequate number of trials are identified, we will carry out analyses for "small-study effects" and publication bias.

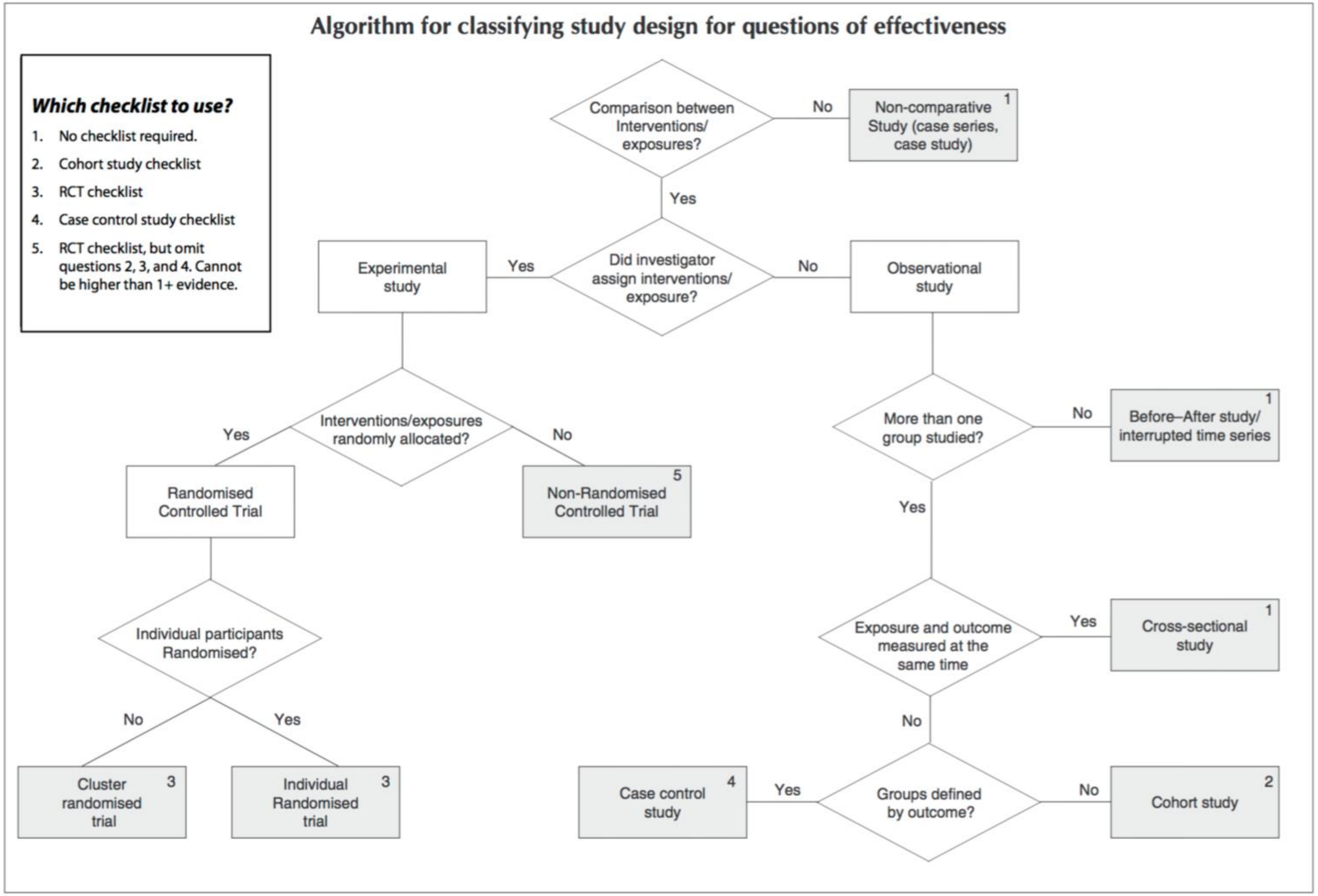
Analysis of subgroups or subsets

If the necessary data are available, subgroup analysis will be performed.

Dissemination plans

Yes.

Appendix II. Scottish Intercollegiate Guidelines Network (SIGN) algorithm for classifying study design for questions of effectiveness



Adapted from NICE (www.nice.org.uk)

Appendix III. Strategy for database search [until October 1st, 2017].

Database	Search strategy
MEDLINE via PubMed http://www.ncbi.nlm.nih.gov/pubmed	(orthodontic* OR malocclusion OR “tooth movement” OR “craniofacial morphology” OR “dentofacial morphology” OR “cranial morphology” OR “facial morphology”) AND (dental OR tooth OR teeth OR enamel) AND (wear OR “tooth wear” OR “occlusal wear” OR abrasion OR attrition OR noncarious OR “non carious” OR non-carious OR lesions OR “surface loss” OR TSL OR NCTSL OR “anterior wear” OR “anterior dental wear” OR “incisal wear”) AND human NOT ((in vitro) AND animal)
Cochrane Central Register of Controlled Trials http://onlinelibrary.wiley.com/cochranelibrary	(orthodontic* OR malocclusion OR “tooth movement” OR “craniofacial morphology” OR “dentofacial morphology” OR “cranial morphology” OR “facial morphology”) AND (dental OR tooth OR teeth OR enamel) AND (wear OR “tooth wear” OR “occlusal wear” OR abrasion OR attrition OR noncarious OR “non carious” OR non-carious OR lesions OR “surface loss” OR TSL OR NCTSL OR “anterior wear” OR “anterior dental wear” OR “incisal wear”) AND human NOT ((in vitro) AND animal) in Title, Abstract, Keywords in Trials'
Cochrane Database of Systematic Reviews http://0-ovidsp.tx.ovid.com.amclb.iii.com/sp-3.16.0b/ovidweb.cgi	(orthodontic* OR malocclusion OR “tooth movement” OR “craniofacial morphology” OR “dentofacial morphology” OR “cranial morphology” OR “facial morphology”) AND (dental OR tooth OR teeth OR enamel) AND (wear OR “tooth wear” OR “occlusal wear” OR abrasion OR attrition OR noncarious OR “non carious” OR non-carious OR lesions OR “surface loss” OR TSL OR NCTSL OR “anterior wear” OR “anterior dental wear” OR “incisal wear”) AND human NOT ((in vitro) AND animal) {Including Limited Related Terms}
Scopus https://www.scopus.com/search/form.url?zone=TopNavBar&origin=searchbasic	(TITLE-ABS-KEY (orthodontic* OR malocclusion OR "tooth movement" OR "craniofacial morphology" OR "dentofacial morphology" OR "cranial morphology" OR "facial morphology") AND TITLE-ABS-KEY (dental OR tooth OR teeth OR enamel) AND TITLE-ABS-KEY (wear OR "tooth wear" OR "occlusal wear" OR abrasion OR attrition OR noncarious OR "non carious" OR non-carious OR lesions OR "surface loss" OR tsl OR nctsl OR "anterior wear" OR "anterior dental wear" OR "incisal wear")) AND (LIMIT-TO (EXACTKEYWORD , "Human") OR LIMIT-TO (EXACTKEYWORD , "Humans") OR LIMIT-TO (EXACTKEYWORD , "Orthodontics") OR LIMIT-TO (EXACTKEYWORD , "Malocclusion") OR LIMIT-TO (EXACTKEYWORD , "Orthodontic Device")) AND (LIMIT-TO (SUBJAREA , "DENT"))
Web of Science™ http://apps.webofknowledge.com/	TOPIC: ((orthodontic* OR malocclusion OR “tooth movement” OR “craniofacial morphology” OR “dentofacial morphology” OR “cranial morphology” OR “facial morphology”) AND (dental OR tooth OR teeth OR enamel) AND (wear OR “tooth wear” OR “occlusal wear” OR abrasion OR attrition OR noncarious OR “non carious” OR non-carious OR lesions OR “surface loss” OR TSL OR NCTSL OR “anterior wear” OR “anterior dental wear” OR “incisal wear”)) Refined by: WEB OF SCIENCE CATEGORIES: (DENTISTRY ORAL SURGERY MEDICINE) Timespan: All years. Indexes: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI.
Arab World Research Source http://0web.a.ebscohost.com.amclb.iii.com/ehost/search/advanced?sid=ff64c697-1ea0-41dc-9afe-961bc654cd05%40sessionmgr4002&vid=0&hid=4114	(orthodontic* OR malocclusion OR “tooth movement” OR “craniofacial morphology” OR “dentofacial morphology” OR “cranial morphology” OR “facial morphology”) AND (dental OR tooth OR teeth OR enamel) AND (wear OR “tooth wear” OR “occlusal wear” OR abrasion OR attrition OR noncarious OR “non carious” OR non-carious OR lesions OR “surface loss” OR TSL OR NCTSL OR “anterior wear” OR “anterior dental wear” OR “incisal wear”) AND human NOT ((in vitro) AND animal)
ClinicalTrials.gov http://clinicaltrials.gov/	(orthodontic* OR malocclusion OR “tooth movement”) AND (dental OR tooth OR teeth OR enamel) AND (wear OR “tooth wear” OR “occlusal wear” OR abrasion OR attrition)
ProQuest Dissertations and Theses Global http://search.proquest.com/dissertations	ti((orthodontic* OR malocclusion OR “tooth movement” OR “craniofacial morphology” OR “dentofacial morphology” OR “cranial morphology” OR “facial morphology”) AND (dental OR tooth OR teeth OR enamel) AND (wear OR “tooth wear” OR “occlusal wear” OR abrasion OR attrition OR noncarious OR “non carious” OR non-carious OR lesions OR “surface loss” OR TSL OR NCTSL OR “anterior wear” OR “anterior dental wear” OR “incisal wear”))

Appendix IV. Details of risk of bias assessment. [Domains examined: 1: Bias due to confounding 2: Bias in selection of participants, 3: Bias in classification of intervention, 4: Bias due to deviations from intended interventions, 5: Bias due to missing data, 6: Bias in measurement of outcomes, 7: Bias in selection of the reported result]

Study	Rating		Reasons for rating
Kuijpers et al., 2009	**1.**	Serious	Important parameters (like the natural progression of tooth wear with age, gender, malocclusion type, craniofacial morphology, treatment duration, etc.) were not controlled.
	2.	Low	No reason to believe that the selection of the participants was biased.
	3.	Low	No statement about the details of the orthodontic treatment. However, it is clearly mentioned that all the participants had received orthodontic treatment.
	4.	Not applicable	Not applicable
	5.	Not applicable	Not applicable
	6.	Moderate	Inherent limitations exist in the procedure of standardization and reliability of assessing wear of teeth using grading scales
	7.	Moderate	The outcome measurements and analyses are consistent with an *a priori* plan.
Panos et al., 2011	**1.**	Serious	Important parameters (like the natural progression of tooth wear with age, craniofacial morphology, etc.) were not controlled.
	2.	Low	No reason to believe that the selection of the participants was biased.
	3.	Low	"All had received comprehensive orthodontic treatment by means of stainless steel appliances in both dental arches. The treatment protocol included two maxillary premolar extractions in eight patients and four premolar extractions (one in each quadrant) in two patients, while 20 individuals were treated without extraction"
	4.	Not applicable	Not applicable
	5.	Not applicable	Not applicable
	6.	Low	"Scanning and digitizing was performed with OrthoProof using a FlashCT (Hytecinc), a high-speed 3D x-ray scanning system for nondestructive internal and external inspection of objects that produces high-resolution images." "The magnitude of the method error was 0.19 mm^3."
	7.	Moderate	The outcome measurements and analyses are consistent with an *a priori* plan.
Park et al., 2014	**1.**	Serious	Important parameters (like the natural progression of tooth wear with age, etc.) were not controlled.
	2.	Low	No reason to believe that the selection of the participants was biased.
	3.	Low	"The sample consisted of dental casts obtained from 56 patients … who received orthodontic treatment with extraction of four premolars…"
	4.	Not applicable	Not applicable
	5.	Not applicable	Not applicable
	6.	Low	"To evaluate tooth wear, the 3D images of the canines at T1 and T2 were superimposed using the best-fit method." "The method error of the measurements was found to be 0.2 mm^3."
	7.	Moderate	The outcome measurements and analyses are consistent with an *a priori* plan.