The association between erosive toothwear and gastro-oesophageal reflux-related symptoms and disease: a systematic review and meta-analysis.

The association between erosive toothwear and gastro-oesophageal reflux-related symptoms and disease: a systematic review and meta-analysis.

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ABSTRACT

Objectives: To conduct a systematic review and meta-analysis to explore the association between erosive toothwear and gastro-oesophageal reflux disease or symptoms (GERD/S).

Sources: Electronic searches were performed in Scopus, Embase, and Web of Science databases for the identification of relevant studies, from 1980 until 2nd August 2019.

Study selection: The review protocol was registered on PROSPERO (CRD42018096959) and the review was conducted according to PRISMA guidelines. Observational studies which examined the association between erosive toothwear and GERD/S were included and categorised according to the use of objective or subjective measures of GERD/S. Where possible, odds ratios (OR) and 95% confidence intervals (CI) were derived and pooled in a meta-analyses.

Data: 27 studies were considered relevant for the qualitative synthesis and 19 studies were pooled. Significantly increased odds of erosive toothwear were observed in individuals with GERD/S. This trend was more strongly associated with objectively measured GERD/S (OR 4.13, 95% CI 1.68-10.13), compared to subjectively measured GERD/S (OR 2.69, 95% CI 1.13-6.38). Whilst heterogeneity was very high these trends remained in most sensitivity and subgroup analyses conducted.

Conclusion: Individuals with GERD/S have a 2-4 fold increased odds ratio of also presenting with evidence of erosive toothwear compared with individuals who do not have GERD/S.

Clinical significance: This review suggests the need for a multidisciplinary medical and dental approach to managing individuals who present with erosive toothwear or GERD/S. Timely referrals between oral health services and gastroenterology should be considered as part of effective diagnosis and management.

Keywords: Erosive toothwear, gastro-oesophageal reflux disease, epidemiology, systematic review, meta-analysis.

1. Introduction

Gastro-oesophageal reflux is a brief physiologic event that can occur several times daily in a normal individual after large meals, without any symptomatic manifestations or complications (1). However gastro-oesophageal reflux disease or symptoms (GERD/S) is characterised by frequent gastric reflux which can cause troublesome symptoms, including heartburn, and is a recognised risk factor for oesophageal adenocarcinoma (2–4). Evidence suggests that toothwear is a frequently reported extra-oesophageal symptom of GERD/S (5). Characterised by aetiology, toothwear can be classified as abrasion, attrition or erosion but is often multifactorial in nature (6). Abrasion results from the interaction between teeth and a foreign object whilst attrition is due to contact between teeth, most often related to clenching and grinding. Erosive toothwear is defined as an irreversible loss of tooth structure caused by chemical acidic action without any bacterial involvement (7). The source of the acid can be intrinsic, including gastro-oesophageal reflux or extrinsic and can be further exacerbated by reduced saliva flow (8,9) and supine positioning when sleeping (10). Studies suggest that an intraoral pH below 5.5 can initiate the dissolution of the superficial enamel layer and may lead to erosive toothwear as well as hypersensitivity of the teeth and mucositis (7,8). Erosive toothwear is common as epidemiological studies estimate the average prevalence of erosive toothwear worldwide ranges from 30-50%, reflecting the magnitude of this disease [8,11,12].

Previous evidence has suggested that the prevalence of GERD/S in patients with erosive toothwear ranges between 25% and 80% (5,11,12). This wide variation in reported prevalence can be explained by differing study designs, inconsistent comparisons among different demographics and varying diagnostic criteria (5,12). To date, beyond the systematic review by Pace *et al*. (13) which highlighted the prevalence of erosive toothwear in individuals with GERD/S, no previous meta-analyses have quantified the odds of erosive toothwear within individuals with GERD/S, compared to non-GERD/S individuals.

Therefore, the aim of this systematic review and meta-analysis was to screen and pool the available evidence to explore the association between erosive toothwear and GERD/S.

2. Materials and methods

2.1 Protocol and registration

This systematic review and meta-analysis were conducted and reported according to PRISMA guidelines (14). A protocol was developed (CRD42018096959) and submitted to PROSPERO: (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=96959). The systematic review protocol described the intention to study the bidirectional relationship between erosive toothwear and GERD/S. However, as the vast majority of studies only presented information on erosive toothwear prevalence in GERD/S individuals (and not vice versa) it was decided to restrict the reporting of review results to the risk of erosive toothwear in GERD/S individuals.

2.2 Data sources and search strategy

Ovid MEDLINE, Scopus, Embase, and Web of Science electronic databases were systematically searched from 1980 until 2nd August 2019. The grey literature was hand searched for records that were not electronically accessible or for those manuscripts without an electronic abstract. Further searches were undertaken to cross check references not available in the electronic databases. The search strategy included terms for erosive toothwear combined with terms for GERD/S, as detailed in Supplementary Table 1. Using controlled keywords, this systematic review combined search terms and synonyms related to erosive toothwear, including tooth abrasion OR tooth attrition OR tooth erosion OR dentin sensitivity OR tooth wear OR toothwear OR crown lengthening, AND terms for reflux including reflux OR heartburn OR acid reflux* OR gastro-oesophageal reflux disease OR gastroesophageal reflux disease OR Barrett*? oesophagus* OR ?esophageal neoplasm OR (?esophag* adj5 (cancer* or adenocarcinoma*)). This systematic review included two types of studies: cross-sectional and case-control, which analysed the association between erosive toothwear and GERD/S. The search was limited to humans, adults and publications in the English language.

2.3 Study selection and eligibility criteria

Articles identified using the search strategy were imported to COVIDENCE systematic review software, (Covidence, Melbourne, Australia) (15). Using this software, duplicates were removed, and two independent reviewers (H.J. and H.C.) screened all titles and abstracts. Potentially relevant full-text articles were then read to determine if an article met the inclusion criteria as outlined in Figure 1. A discussion between the two reviewers was held to reach an agreement and a third reviewer (GMK) was available to resolve disagreements (however this was not necessary). In order to test agreement between

the first and second reviewers, kappa values were calculated at each stage of data extraction. The kappa scores for 'Records after duplicates removed and screened' was K=1.0; 'Full-text articles assessed for eligibility' K=0.89; for 'Studies included in the qualitative synthesis' K=0.80; 'Studies included in quantitative synthesis' K=1.0. Each article excluded at the full-text review stage was justified, as demonstrated in Figure 1.

2.4 Inclusion and exclusion criteria

All human studies performed in a population aged 15 years and over which included a dental assessment (oral examination or self-reported dental symptoms) and a gastro-oesophageal assessment for reflux symptoms or disease (endoscopic assessment or self-reported symptoms) were eligible for inclusion. To facilitate data synthesis, studies with self-reported symptoms were categorised as subjectively measured GERD/S whilst those including endoscopic assessment (including 24-hour pH manometry tests) were termed objectively measured GERD/S. Case reports and studies with a population only including patients with eating disorders such as anorexia nervosa, bulimia nervosa or rumination disorder, were excluded. This information is further detailed in Supplementary Table 1.

2.5 Data extraction and study quality assessment

Data was extracted relating to study design, geographic location, year of publication, sample size, age, case and control definition of GERD/S, case and control definition of erosive toothwear, the assessment method for erosive toothwear and the assessment method for GERD/S, adjusted confounders and outcomes. As described previously for the purpose of data synthesis, it was decided post-hoc to dichotomise the studies according to the GERD/S measurement into: (i) objectively measured GERD/S and (ii) subjectively measured GERD/S.

Information on the clinical diagnoses of erosive toothwear was recorded including the use of clinical indices as illustrated in Supplementary Table 2.

The Newcastle Ottawa scale (NOS) was utilised to assess the quality of evidence reported from cross-sectional (21) and case-control studies (22), respectively. The NOS for cross-sectional study design was adapted from NOS for cohort studies.

2.6 Statistical analysis

Review Manager (RevMan Version 5.3, The Cochrane Collaboration) was used to perform a random-effects meta-analysis to produce pooled estimates from odds ratios (OR) and 95% confidence intervals (CI) of included studies, to test the association between erosive toothwear and GERD/S, where possible. However several studies did not provide this information and OR and 95% CI were calculated from prevalence data reported in the study. Separate meta-analyses were conducted for objectively and subjectively measured GERD/S studies. The I^2 statistic was applied to determine the extent of heterogeneity in the studies included within the meta-analyses (23). A funnel plot was generated to visually assess the potential for publication bias.

Sensitivity analyses were performed by excluding individual studies one at a time with the intention of assessing the robustness of the pooled data. In accordance with the protocol, sensitivity and subgroup analyses were conducted for study populations by geographic locations, excluding studies which reported on individuals with specific health conditions or characteristics, and by systematically excluding individual studies in order to assess the effect on the pooled result estimates and observing the heterogeneity. Although subgroup analyses according to sex and age categories were planned in the protocol, insufficient detail was presented in individual studies to enable such analyses.

3. Results

The initial search strategy identified 785 articles which was reduced to 457 articles after duplicates were removed. Fifty-six articles met the criteria for full text assessment where a further 29 articles were excluded. In total, 27 original articles were considered relevant for the qualitative synthesis, representing a population sample of n=8565 (5374 controls and 3191 individuals with GERD/S) (Figure 1).

3.1 Erosive toothwear in individuals with GERD/S

Of the 27 studies included, 15 studies provided data on objectively measured GERD/S and 12 studies provided data on subjectively measured GERD/S (Tables 1, 2). However, only 19 studies reported sufficient information to facilitate data pooling; n=9 for objectively measured GERD/S and n=10 for subjectively measured GERD/S. When the 19 studies reporting objectively or subjectively measured GERD/S were combined, the analysis revealed a 3.3-fold increased odds of erosive toothwear in individuals with GERD/S, compared with controls without GERD/S (OR 3.29, 95% CI 1.80-6.02, I^2 =95%) (Figure 2).

3.2 Erosive toothwear in individuals with objectively measured GERD/S

Fifteen studies (7,8,10–12,19,20,24–31) evaluated the prevalence of erosive toothwear in individuals with objectively measured GERD/S (Table 1). Of these, ten studies (8,10–12,19,20,25,27,30,31) confirmed the diagnosis of GERD/S using clinical symptoms, endoscopic assessment and a 24-hour pH manometry test (the gold standard for GERD assessment). Five studies (7,24,26,28,29) determined GERD/S using clinical symptoms, and endoscopy examination to prove mucosal breaks within the oesophagus.

Erosive toothwear (referred to as tooth or dental erosion in most studies) was assessed via dental examination in all studies, although a variety of methods were used to assess the severity of erosive toothwear (Table 1). The underlying definitions for each of the erosive toothwear criteria applied are summarised in Supplementary Table 2. All studies compared GERD/S individuals with control populations who had no evidence of GERD/S. The NOS quality assessment scores varied from 4 to 7 stars (Table 1).

Nine studies (11,12,19,24,26,27,29–31) which assessed the prevalence of erosive toothwear in participants with objectively measured GERD/S were eligible to be included in the pooled analysis. Only one study (24) presented an OR for the prevalence of toothwear in GERD/S individuals which was adjusted for other key confounders. The reported prevalence of erosive toothwear in individuals in the remaining studies was used to calculate unadjusted odds ratios where possible. The meta-analysis indicated

increased odds of erosive toothwear in individuals with GERD/S (pooled OR 4.13, 95% CI 1.68- 10.13), with accompanying high heterogeneity (I^2 = 85%), as shown in Figure 2.

3.3 Erosive toothwear in individuals with subjectively measured GERD/S

Twelve studies (6,16,17,32–40) assessed the prevalence of erosive toothwear in individuals with GERD/S, based on self-completed questionnaires, as detailed in Table 2. In general, these studies were of the cross-sectional design. The NOS quality assessment of score for these studies varied from 3 to 7 stars (Table 2). The erosive toothwear assessment was completed according to several assessment criteria (Supplementary Table 2) by trained health professionals. Erosive toothwear was often reported under different synonyms within these studies, including tooth wear, dental erosion, dentine sensitivity, non-carious cervical lesions and tooth surface loss. As shown in Table 2, approximately half of these studies adjusted for confounders including age, sex/gender, education, dietary intake, oral health habits and socioeconomic status (6,16,17,32,36,38,40). Where odds ratios were not presented, these were calculated where possible from the data provided.

Ten studies were eligible to be pooled in a meta-analysis (6,16,17,32,34–37,39,40). The meta-analysis illustrated 2.7-fold increased odds of erosive toothwear in individuals with subjectively measured GERD/S, compared with controls (pooled OR 2.69, 95% CI 1.13-6.38). However, a high degree of heterogeneity in between-study results was observed in this analysis (I^2 = 97%), as shown in Figure 2.

Two studies, Wan Nik *et al.* (38) and Smith *et al.* (33), provided data on subjectively measured GERD/S, but were not included in the pooled data due to not presenting sufficient data to enable calculation of an odds ratio. The first study analysed GERD/S and erosive toothwear in Sjogren's syndrome patients (38). Patients in the Sjogren's syndrome group (n=33) reported a higher prevalence of GERD/S and a higher percentage of surfaces with toothwear ($p < 0.001$) compared with 20 healthy controls (38). The second study investigated the prevalence and severity of non-carious cervical lesions (13.1%) in 156 individuals (33). This study demonstrated a positive but non-significant association between non-carious cervical lesions and heartburn (OR 1.6, CI 0.3-8.7) and gastric reflux (OR 1.2, CI 0.3-5.2) (33).

3.4 Sensitivity and sub-group analysis

Sensitivity analyses were conducted separately for two the groups, (i) objectively and (ii) subjectively measured GERD/S by sequentially excluding individual studies (Table 3). The direct association between

erosive toothwear and GERD/S outcomes remained significant in most analyses, with little impact on the levels of high heterogeneity observed, suggesting is was not attributable to any individual study.

Further subgroup analyses were conducted based on geographic location of the study populations, including Europe, North America, Asia and Africa, as illustrated in supplementary table 3. The subgroup analysis of ten European studies revealed a slightly attenuated association between erosive toothwear and GERD/S (OR 2.14, 95% CI 0.86-5.32) with high heterogeneity (I^2=97%), compared with the main analysis pooling all 19 studies (OR 3.29, 95% CI 1.80-6.09). In contrast, the pooled result of four North American studies demonstrated a greater association between erosive toothwear and GERD/S, although this generated extremely large confidence intervals (OR 11.52, 95% CI 1.06-125.50) with I^2=90%. The subgroup analysis of four Asian studies and one African study revealed positive associations consistent with those observed in the main analysis with the lower levels of heterogeneity (I^2=59 %).

Finally, sensitivity analyses were performed by excluding studies in which the population was considered to have specific characteristics or health conditions. From the studies in which GERD/S was objectively measured, two focussed on populations with specific health conditions; Saeves *et al.* (19) and Bohmer *et al.* (11), who reported toothwear in patients with Prader-Willi syndrome and in intellectually disabled adults, respectively (Table 3). Of the pooled studies in which GERD/S was subjectively measured, three analysed distinct populations (Table 3); the study by Teixeira *et al.* (17) investigated institutionalised alcoholic patients, Antunes *et al.* (34) included amateur runners and Li *et al.* (40) investigated individuals with bruxism. The pooled meta-analyses following exclusion of these studies generated an OR of 4.48 (95% CI 1.51-13.29) for the objectively measured GERD/S group and an OR of 3.30 (95% CI 1.16-9.39) for the subjectively measured GERD/S group.

A funnel plot was produced to visually assess publication bias, as shown in Figure 3. The plot is symmetrical and thus did not suggest publication bias in studies reporting on the association between erosive toothwear and GERD/S.

4. Discussion

This systematic review and meta-analyses clearly demonstrate that individuals with GERD/S are at increased odds of presenting with erosive toothwear when compared to controls without GERD/S. The positive association between erosive toothwear and GERD/S in adult participants in this systematic review is consistent with the findings of a previous systematic review published by Pace *et al.* in 2008 (13). Their review included 17 articles and included a combination of 6 original studies on children and 11 studies in adult populations (13). Only seven studies in the previous systematic review estimated the prevalence of erosive toothwear in adults and this varied from 5-47.5% (mean=32.5%) in individuals with GERD/S. The other four studies did not have a corresponding control group and observed the prevalence of GERD/S in adult patients with dental erosion only. From the seven adult studies of the Pace *et al*. review, three were included in the current meta-analysis (10,12,26) while four studies (41–44) were excluded. One study was excluded due characteristics of the study population (41) and the other three studies did not include control groups (42–44). The Pace *et al.* review did not calculate prevalence estimates as related to controls, and therefore these results cannot be compared with the odds ratios generated for the purposes of this review (13).

This review adds to previous literature by including a novel meta-analysis which formally highlights the increased odds of erosive toothwear in individuals with GERD/S compared with non-GERD/S populations. The meta-analysis illustrated a stronger association with erosive toothwear in the objectively measured GERD/S group (OR=4.1) compared with the subjectively measured group (OR=2.7). Interestingly, Wilder-Smith *et al.* illustrated the improved accuracy of objective tests for GERD/S compared to reported or subjective symptoms in a previous study(5). The authors conclude that objective measures are more reliable than subjectively reported symptoms by participants when making a diagnosis of GERD/S.

There are biologically plausible explanations for the greater risk of erosive toothwear in individuals with GERD/S than for non-GERD/S populations. Erosive toothwear can arise through repeated exposure to gastric acid over a prolonged timeframe which may dissolve tooth enamel (7,32). Patients with GERD/S commonly present reduced tone of the lower oesophageal sphincter, which when combined with peristaltic movement of the oesophagus and supine positioning, potentiate the backflow of the gastric content to the oesophagus and/or the mouth and airways (25). The severity of erosive toothwear has previously been demonstrated to be directly correlated with the frequency and duration of GERD/S (25). This is supported by the work of Wilder-Smith *et al.* which demonstrated that individuals with reflux-

related dental erosion lose significantly less enamel thickness (Mean loss=0.3%) after treatment with a proton pump inhibitor compared to a placebo (Mean loss=0.08%, p=0.013) (45).

GERD/S and bruxism are two interrelated factors which can further contribute to erosive toothwear (40). Bruxism is a 'stereotyped movement disorder characterised by tooth grinding and/or clenching during sleep' (46). According to Ohmure and colleagues, the lower pH of the oesophagus can act as a trigger for bruxism which consequently intensifies the erosive toothwear process (46). In an experimental study it was observed that adults exposed to intra-oesophageal acid infusion had significantly higher recorded episodes of bruxism compared with controls exposed to saline solution (46). In that study, bruxism was diagnosed by polysomnography with electromyogram of the masseter muscle, oesophageal pH monitoring and video recording (46).

GERD/S is a potential risk factor for reflux esophagitis, Barrett's oesophagus and oesophageal adenocarcinoma (2). Whilst esophagitis is the most common complication of GERD/S, such conditions are diagnosed after endoscopic examination including GERD/S stage or severity (2). Currently, endoscopic examination is not routinely recommended for patients with erosive toothwear due to high costs and patient discomfort (47). Evidence suggests that erosive toothwear may negatively impact the quality of life of patients with GERD/S. According to the World Health Organisation, oral health is recognised as an essential contributor to the general health of an individual, with significant impacts on the overall quality of life (48,49). As such, there have been calls for governments to prioritise policies to improve oral health and access to oral health services (50). However, to our knowledge, such recommendations have not yet been extended to GERD/S patients. This is illustrated by the National Institute of Clinical Excellence (NICE) United Kingdom guidelines for management of GERD/S where there is only a recommendation to "recognise" dental erosion "as a possible complication of gastro-oesophageal reflux in infants, children and young people" (49), with no equivalent statement in guidelines for adults with GERD/S (51). Given the findings of the current review, further attention to the oral health consequences of GERD/S is warranted.

This systematic review has several strengths. Robust systematic review methodology was applied to both the study selection and data extraction in line with PRISMA guidelines. Novel meta-analyses were performed, estimating the odds of erosive toothwear in individuals with GERD/S for the first time in the adult population. The review included 27 studies from a range of geographic locations, helping us to

comprehend more precisely the magnitude of erosive toothwear in GERD/S patients worldwide. The dental assessments to evaluate erosive toothwear across studies was of a high standard and almost all were performed by trained dentists or health professionals according to standardised criteria (Supplementary Table 2).

Nonetheless, a number of potential limitations of the review must be acknowledged. Firstly, the studies included may have suffered from recall bias in the subjectively measured GERD/S population group, in which questionnaires or interviews were used to assess symptoms such as heartburn, reflux and pyrosis (16). However, we have attempted to overcome this somewhat by separately considering these results from the studies of objectively measured GERD/S. Indeed, the magnitude of the association in the latter studies was higher than that observed in subjectively measured GERD/S patient studies, suggesting that any recall bias only served to reduce the likelihood of detecting an association. Secondly, the majority of studies included in the meta-analyses had high levels of heterogeneity, suggesting that caution is required when interpreting the results. Although we attempted to account for this heterogeneity, it did not appear to be attributed to differing measurement methods of GERD/S, geographic location of studies, the exclusion of studies in distinct population groups or any individual study. Thirdly, the cross-sectional study design of several studies means that the temporal relationship between GERD/S and erosive toothwear could not be assessed, and few studies adjusted for known confounders. However, this does not affect the primary aim of our review, which did not seek to evaluate aetiology but wished to estimate the magnitude of erosive toothwear odds in GERD/S patients. Finally, our systematic review was restricted to publications in the English language and therefore it is possible that we have missed relevant literature published in other languages.

5. Conclusion

In summary, the results of this systematic review and meta-analysis indicate that individuals with GERD/S have a 2-4 fold increased odds ratio of also presenting with evidence of erosive toothwear compared with individuals who do not have GERD/S. Therefore, the promotion of appropriate preventive dental care should be considered for individuals with GERD/S, including timely referrals to oral health service colleagues from gastroenterology and vice-versa.

Conflict of interest

The authors declare no conflict of interest.

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References

[1] P.V. Dicpinigaitis, Chronic Cough Due to Gastroesophageal Reflux Disease ACCP Evidence-Based Clinical Practice Guidelines, Chest. 129 (2006) 80S-94S.

[2] N. Vakil, The Montreal Definition and Classification of Gastroesophageal Reflux Disease: A Global Evidence-Based Consensus, Ther Res. 27 (2006) 805-812.

[3] J.E. Richter, J.H. Rubenstein, Presentation and Epidemiology of Gastroesophageal Reflux Disease, Gastroenterology. 154 (2018) 267-276.

[4] F. Schlottmann, D. Molena, M.G. Patti, Gastroesophageal reflux and Barrett's esophagus: a pathway to esophageal adenocarcinoma, Updates Surg. 70 (2018) 339-442.

[5] C.H. Wilder-Smith, A. Materna, L. Martig, A. Lussi, Gastro-oesophageal reflux is common in oligosymptomatic patients with dental erosion: A pH-impedance and endoscopic study, United Eur Gastroenterol J. 3 (2015) 174-181.

[6] Z. Wei, Y. Du, J. Zhang, B. Tai, M. Du, H. Jiang, Prevalence and indicators of tooth wear among Chinese adults, PLoS One. 11 (2016) 1-14.

[7] M.A. Garcia Santos Silva, J.H. Damante, A.C. Marconi Stipp, M.M. Tolentino, P.R. Carlotto, R.N. Fleury, Gastroesophageal reflux disease: New oral findings, Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 91 (2001) 301-310.

[8] M.C.C.S.F. Correa, M.M. Lerco, M. de L. R. de S. Cunha, M.A.C. de A. Henry, Salivary parameters and teeth erosions in patients with gastroesophageal reflux disease, Arq Gastroenterol. 49 (2012) 214-218.

[9] A. Preetha, D. Sujatha, B.A.H.S. Patil BA, Oral manifestations in gastroesophageal reflux disease, Gen Dent. 63 (2015) 27-31.

[10] R. Moazzez, D. Bartlett, A. Anggiansah, Dental erosion, gastro-oesophageal reflux disease and saliva: How are they related?, J Dent. 32 (2004) 489-494.

[11] C.J. Böhmer, E.C. Klinkenberg-Knol, M.C. Niezen-de Boer, P.R.M.S. Meuwissen, Dental erosions and gastro-oesophageal reflux disease in institutionalized intellectually disabled individuals, Oral Disease J. 3 (1997) 272-275.

[12] J.V. Muñoz, B. Herreros, V. Sanchiz, C. Amoros, V. Hernandez, I. Pascual, et al., Dental and periodontal lesions in patients with gastro-oesophageal reflux disease, Dig Liver Dis. 35 (2003) 461-467.

[13] F. Pace, S. Pallotta, M. Tonini, N. Vakil, G. Bianchi Porro G, Systematic review: Gastro-oesophageal reflux

disease and dental lesions, Aliment Pharmacol Ther. 27 (2008) 1179-1186.

[14] J.M. Miguelena Bobadilla, M. Gil Albiol, J. Escartín Valderrama, J.I. Barranco Domínguez, Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement, Nutr Hosp 18 (2003) 264-268.

[15] J. Babineau, Product Review: Covidence (Systematic Review Software), J Can Heal Libr Assoc / J l'Association des bibliothèques la santé du Canada. 35 (2014) 68.

[16] V. Alaraudanjoki, M.L. Laitala, L. Tjäderhane, P. Pesonen, A. Lussi, J. Ronkainen, et al., Influence of Intrinsic Factors on Erosive Tooth Wear in a Large-Scale Epidemiological Study, Caries Res. 50 (2016) 508-516.

[17] L. Teixeira, M.C. Manso, P. Manarte-Monteiro, Erosive tooth wear status of institutionalized alcoholic patients under rehabilitation therapy in the north of Portugal, Clin Oral Investig. 21 (2017) 809-819.

[18] Y. Kitasako, Y. Sasaki, T. Takagaki, A. Sadr, J. Tagami, Age-specific prevalence of erosive tooth wear by acidic diet and gastroesophageal reflux in Japan, J Dent. 43 (2015) 418-423.

[19] R. Saeves, F. Strøm, L. Sandvik, H. Nordgarden, Gastro-oesophageal reflux - An important causative factor of severe tooth wear in Prader-Willi syndrome?, Orphanet J Rare Dis. 13 (2018) 1-7.

[20] U. Kaczmarek, D. Waśko-Czopnik, M. Kowalczyk-Zając, L. Paradowski, The influence of reflux disease on selected components of saliva and occurrence of dental erosion, Gastroenterologia Polska. 11 (2004) 109-114.

[21] P.A. Modesti, Cross sectional study Newcastle- Ottawa quality assessment scale, PLoS One. 11 (2016) 1-2.

[22] A. Stang, Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses, Eur J Epidemiol. 25 (2010) 603-605.

[23] J.P.T. Higgins, S.G. Thompson, Quantifying heterogeneity in a meta-analysis, Stat Med. 21 (2002)1539-1558.

[24] W. Li, J. Liu, S. Chen, Y. Wang, Z. Zhang, Prevalence of dental erosion among people with gastroesophageal reflux disease in China, J Prosthet Dent. 117 (2017) 48-54.

[25] R. Moazzez, A. Anggiansah, D.W. Bartlett, The association of acidic reflux above the upper oesophageal sphincter with palatal tooth wear, Caries Res. 39 (2005) 475-478.

[26] A.O. Oginni, E.A. Agbakwuru, D.A. Ndububa, The prevalence of dental erosion in Nigerian patients with gastro-oesophageal reflux disease, BMC Oral Health. 5 (2005) 1-6.

[27] L. Roesch-Ramos, F. Roesch-Dietlen, J.M. Remes-Troche, G. Romero-Sierra, C.J. de Mata-Tovar, A.A.

Azamar-Jácome, et al., Dental erosion, an extraesophageal manifestation of gastroesophageal reflux disease. The experience of a center for digestive physiology in southeastern Mexico, Rev Esp Enfermedades Dig. 106 (2014) 17-25.

[28] H. Yoshikawa, K. Furuta, M. Ueno, M. Egawa, A. Yoshino, S. Kondo S, et al., Oral symptoms including dental erosion in gastroesophageal reflux disease are associated with decreased salivary flow volume and swallowing function, J Gastroenterol. 47 (2012) 412-420.

[29] A. Ramachandran, S. Raja Khan, N. Vaitheeswaran, Incidence and pattern of dental erosion in gastroesophageal reflux disease patients, Journal of Pharmacy And Bioallied Sciences. 9 (2017) 138-141.

[30] O. Di Fede, C. Di Liberto, G. Occhipinti, S. Vigneri, L. Lo Russo, S. Fedele, et al., Oral manifestations in patients with gastro-oesophageal reflux disease: A single-center case-control study, J Oral Pathol Med. 37 (2008) 336-340.

[31] T. Jensdottir, I.B. Arnadottir, I. Thorsdottir, A. Bardow, K. Gudmundsson, A. Theodors, et al., Relationship between dental erosion, soft drink consumption, and gastroesophageal reflux among Icelanders, Clin Oral Investig. 8 (2004) 91-96.

[32] N. X. West, M. Sanz, A. Lussi, D. Bartlett, P. Bouchard, D. Bourgeois, Prevalence of dentine hypersensitivity and study of associated factors: A European population-based cross-sectional study, J Dent. 41 (2013) 841-851.

[33] W.A.J. Smith, S. Marchan, R.N.Rafeek, The prevalence and severity of non-carious cervical lesions in a group of patients attending a university hospital in Trinidad, J Oral Rehabil. 35 (2008) 128-134.

[34] L.S. Antunes, L. Veiga, V.S. Nery, C.C. Nery, L.A. Antunes, Sports drink consumption and dental erosion among amateur runners, J Oral Sci. 59 (2017) 639-643.

[35] A. Benages, J.V. Muñoz, V. Sanchiz, F. Mora, M. Mínguez, Dental erosion as extraoesophageal manifestation of gastro-oesophageal reflux, Gut. 55 (2006) 1050-1051

[36] D.C. Milani, A.P.C. Venturini, S.M. Callegari-Jacques, F. Fornari, Gastro-oesophageal reflux disease and dental erosions in adults: Influence of acidified food intake and impact on quality of life, Eur J Gastroenterol Hepatol. 28 (2016) 797-801.

[37] D. Tantbirojn, M.R. Pintado, A. Versluis, C. Dunn, R. Delong, Quantitative analysis of tooth surface loss associated with gastroesophageal reflux disease: A longitudinal clinical study, J Am Dent Assoc. 143 (2012) 278-85

[38] W.N.N. Wan Nik, A. Banerjee, R. Moazzez, Gastro-oesophageal reflux disease symptoms and tooth wear in

patients with Sjogren syndrome, Caries Res. 45 (2011) 323-326.

[39] I. Stojšin, T. Brkanić, S. Živković, Reflux disease as an etiological factor of dental erosion, Srp Arh Celok Lek. 138 (2010) 292-296.

[40] Y. Li, F. Yu, L. Niu, W. Hu, Y. Long, F. Tay, et al., Associations among Bruxism, Gastroesophageal Reflux Disease, and Tooth Wear, J Clin Med. 7 (2018) 417-428.

[41] R.J.L.F. Loffeld, Incisor teeth status in patients with reflux oesophagitis, Digestion. 57 (1996) 388-390.

[42] P.L. Schroeder, S.J. Filler, B. Ramirez, D.A. Lazarchik, M.F. Vaezi, J.E. Richter, Dental erosion and acid reflux disease, Ann Intern Med. 122 (1995) 809-815.

[43] V. Järvinen, J.H. Meurman, H. Hyvärinen, I. Rytömaa, H. Murtomaa, Dental erosion and upper gastrointestinal disorders. Oral Surgery, Oral Med Oral Pathol. 65 (1988) 298-303.

[44] J.H. Meurman, J. Toskala, P. Nuutinen, E. Klemetti, Oral and dental manifestations in gastroesophageal reflux disease, Oral Surgery, Oral Med Oral Pathol. 78 (1994) 583-589.

[45] C.H. Wilder-Smith, P. Wilder-Smith, H. Kawakami-Wong, J. Voronets, K. Osann, A. Lussi, Quantification of dental erosions in patients with GERD using optical coherence tomography before and after double-blind, randomized treatment with esomeprazole or placebo, Am J Gastroenterol. 104 (2009) 2788-2795.

[46] H. Ohmure, K. Oikawa,K. Kanematsu, Y. Saito, T. Yamamoto, H. Nagahama, et al., Influence of experimental esophageal acidification on sleep bruxism: A randomized trial, J Dent Res. 90 (2011) 665-671.

[47] E.C. Smyth, J. Lagergren, R.C. Fitzgerald, F. Lordick, M.A. Shah, P. Lagergren et al., Oesophageal Cancer Europe PMC Funders Group. 2018

[48] P.E. Petersen, Priorities for research for oral health in the 21st century--the approach of the WHO Global Oral Health Programme, Community Dent Health. 22 (2005) 71-74.

[49] NICE, Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people, Natl Inst Heal Care Excell. 55 (2015) 1-36.

[50] Royal College of Surgeons, Actions for the government to improve oral health. Faculty of Dental Surgery (2015) 1-12.

[51] NICE, Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management, (2019).

[52] A. Dundar, A. Sengun, Dental approach to erosive tooth wear in gastroesophageal reflux disease, Afr Health Sci. 14 (2014) 481-486.

[53] I. Strużycka, A. Lussi, A. Bogusławska-Kapała, E. Rusyan, Prevalence of erosive lesions with respect to risk

factors in a young adult population in Poland-a cross-sectional study, Clin Oral Investig. 21 (2017) 2197-2203.

[54] S. Alves Mdo, F. da Silva, S.G. Araujo, C. de Carvalho, M. Santos, L. de Carvalho, Tooth wear in patients submitted to bariatric surgery, Braz Dent J. 23 (2012) 160-166.

Table 1. Summary of study characteristics that evaluated the prevalence of erosive toothwear in patients with objectively measured gastro-oesophageal reflux disease/symptoms.

Study-Location-Year	Gastro-oesophageal reflux disease		Erosive toothwear		Adjustment for confounders	NOS [c] Quality score
	Diagnosis mode	No. cases/ controls	Diagnosis criteria at dental examination	No. outcomes cases/controls		
Bohmer et al.[a] Netherlands (1997)	Clinical GERD/ endoscopy/ pH-manometry	29/34	Eccles and Jenkins	19/10	No	7
Correa et al. Brazil (2012)	Clinical GERD/ endoscopy/ pH-manometry	30/30	Eccles and Jenkins	Not reported.	No	7
Fede et al. Italy (2008)	Clinical GERD/ endoscopy/ pH-manometry	200/100	Smith and Knight	18/13	No	7
Jensdottir et al.[b] Iceland (2004)	Clinical GERD/ endoscopy/ pH-manometry	23/57	Lussi	8/23	No	7
Kaczmarek et al. Poland (2004)	Clinical GERD/ endoscopy/ pH-manometry	26/45	Lussi	8	No	4
Li et al. China (2017)	Clinical GERD/ endoscopy/ questionnaire	51/50	Smith and Knight	31/14	Age, sex, dietary factors, smoking	6
Moazzez et al. England (2004)	Clinical GERD/ endoscopy/ pH-manometry	59/76	Smith and Knight	Not reported.	No	7
Moazzez et al. England (2005)	Clinical GERD/ endoscopy/ pH-manometry	31/7	Smith and Knight	9/0	No	6
Munoz et al. Spain (2003)	Clinical GERD/ endoscopy/ pH-manometry	181/72	Eccles and Jenkins	86/9	No	7
Oginni et al. Nigeria (2005)	Clinical GERD/ endoscopy/ questionnaire	125/100	Smith and Knight	20/5	No	5
Ramachandran et al. Saudi Arabia (2017)	Clinical GERD/ endoscopy/ questionnaire	25/25	[d]BEWE	22/8	No	7
Ramos et al. Mexico (2014)	Clinical GERD / endoscopy / pH-manometry	60/60	Eccles and Jenkins	46/2	No	6
Saeves et. Al[e] Norway (2018)	Clinical GERD / endoscopy / pH-manometry	11/5	Visual Erosion dental examination and toothwear index	6/2	No	6
Silva et al. Brazil (2001)	Clinical GERD/ endoscopy / questionnaire	31/ 14	Eccles and Jenkins	1/0	No	6
Yoshikawa et al. Japan (2012)	Clinical GERD/ endoscopy / questionnaire	40/30	Smith and Knight	9/0	No	5

Table 1 legend: [a] The study population was intellectually disabled adults. This study presented prevalence estimates as GERD in tooth erosion/non-erosion groups, and the data extracted for our table was derived from this. [b] The control population for Jensdottir et al. were young adults aged 19-22 years. [c] Newcastle Ottawa Scale. [d] Basic Erosive Wear Examination. [e] The study population was patients with Prader-Willi syndrome.

Table 2. Principal findings from included manuscripts that evaluated the prevalence of erosive toothwear in patients with subjectively measured gastro-oesophageal reflux disease.

Study-Location-Year	Gastro-oesophageal reflux disease		Erosive toothwear		Adjustment for confounders	NOS Quality score
	Diagnosis mode	No. cases/ controls	Diagnosis criteria at dental examination	No. outcomes in cases/controls		
Alaraudanjoki et al. N. Finland (2016)	Questionnaire	1164/699	BEWE	561/323	Sex, alcohol	7
Antunes et al.[(a)] Brazil (2017)	Questionnaire	3/105	Clinical examination	2/19	No	5
Benages et al. Spain (2006)	Questionnaire	181/72	Eccles and Jenkins	86/9	No	6
Li et al.[(b)] China (2018)	Questionnaire	68/658	Smith and Knight	33/191	Age, gender, smoking, alcohol, acidic diet tea consumption,	7
Milani et al. Brazil (2016)	Questionnaire	143/274	Smith and Knight	37/47	Age, gender, acid fruits	7
Tantbirojn et al. USA (2012)	Questionnaire	12/6	Optical scanning (software)	9/1	No	4
Teixeira et al.[(c)] Portugal (2016)	Questionnaire	76/201	Eccles and Jenkins	73/200	Age, alcohol education,	7
Wan Nik et al.[(d)] London (2011)	Questionnaire	22/11	Smith and Knight	No reference	Age, sex	4
Wei et al. China (2016)	Questionnaire	39/681	BEWE	35/568	Age, high frequency of acid drink, chewing unilaterally, low SES	7
West et al. European (2013)	Questionnaire	771/2145	BEWE	473/309	Age, brushing teeth frequency, smoking, gender, fresh fruit intake, isotonic and energy drinks, smoking, occupation	7
Smith et al. Trinidad (2008)	Questionnaire	Not reported.	Clinical examination	Not reported	No	3
Stojsin et al. Serbia (2009)	Questionnaire	30/30	Eccles and Jenkins	23/16	No	4

Table 2 legend: These study populations were [(a)] amateur runners, [(b)] patients with Bruxism, [(c)] institutionalised alcoholic patients and [(d)] patients with Sjogren syndrome. SES: Socioeconomic status.

Table 3. Sensitivity and subgroup analyses of studies that investigate objectively and subjectively measured gastro-oesophageal reflux disease/symptoms and erosive toothwear.

Objectively measured gastro-oesophageal reflux disease/symptoms.				
Studies (references)	Number of studies	Pooled risk estimate (95% CI)	I-squared (%)	p-value
All studies	n=9	4.13 (1.68-10.13)	85%	<0.001
Excluding individual studies				
Excluding Bohmer study (11)	n=8	4.11 (1.49-11.32)	87%	<0.001
Excluding Fede study (30)	n=8	5.30 (2.29-12.25)	78%	<0.001
Excluding Jensdot. study (31)	n=8	5.14 (2.00-13.16)	84%	<0.001
Excluding Li study (24)	n=8	4.20 (1.47-12.01)	87%	<0.001
Excluding Munoz study (12)	n=8	3.92 (1.40-11.02)	86%	<0.001
Excluding Ogini study (26)	n=8	4.24 (1.52-11.78)	87%	<0.001
Excluding Ramach. Study (29)	n=8	3.56 (1.39-9.11)	85%	<0.001
Excluding Ramos study (27)	n=8	2.90 (1.35-6.24)	78%	<0.001
Excluding Saeves study (19)	n=8	4.44 (1.71-11.53)	87%	<0.001
Excluding studies in individuals with specific health conditions or characteristics				
Excluding Bohmer (11) and Saeves (19) studies	n=7	4.48 (1.51-13.29)	88%	<0.001
Subjectively measured gastro-oesophageal reflux disease/symptoms.				
Studies (references)	Number of studies	Pooled risk estimate (95% CI)	I-squared (%)	p-value
All studies	n=10	2.69 (1.13-6.38)	97%	<0.001
Excluding individual studies				
Excluding Alaraud. study (16)	n=9	3.11 (1.45-6.65)	90%	<0.001
Excluding Antunes study (34)	n=9	2.48 (1.02-6.06)	97%	<0.001
Excluding Benages study (35)	n=9	2.41 (0.95-6.13)	97%	<0.001
Excluding Li study (40)	n=9	2.74 (1.04-7.23)	97%	<0.001
Excluding Milani study (36)	n=9	2.86 (1.09-7.51)	97%	<0.001
Excluding Stojsin study (39)	n=9	2.67 (1.06-6.72)	97%	<0.001
Excluding Tantbir. Study (37)	n=9	2.41 (0.99-5.87)	97%	<0.001
Excluding Teixeira study (17)	n=9	3.35 (1.38-8.13)	97%	<0.001
Excluding Wei study (6)	n=9	2.83 (1.12-7.13)	97%	<0.001
Excluding West study (32)	n=9	2.16 (1.25-3.73)	79%	<0.001
Excluding studies in individuals with specific health conditions or characteristics				
Excluding Antunes (34) Li (40) and Teixeira (17) studies	n=7	3.30 (1.16-9.39)	98%	<0.001

Figure 1. Flow chart of the selection of publications included in the meta-analysis.

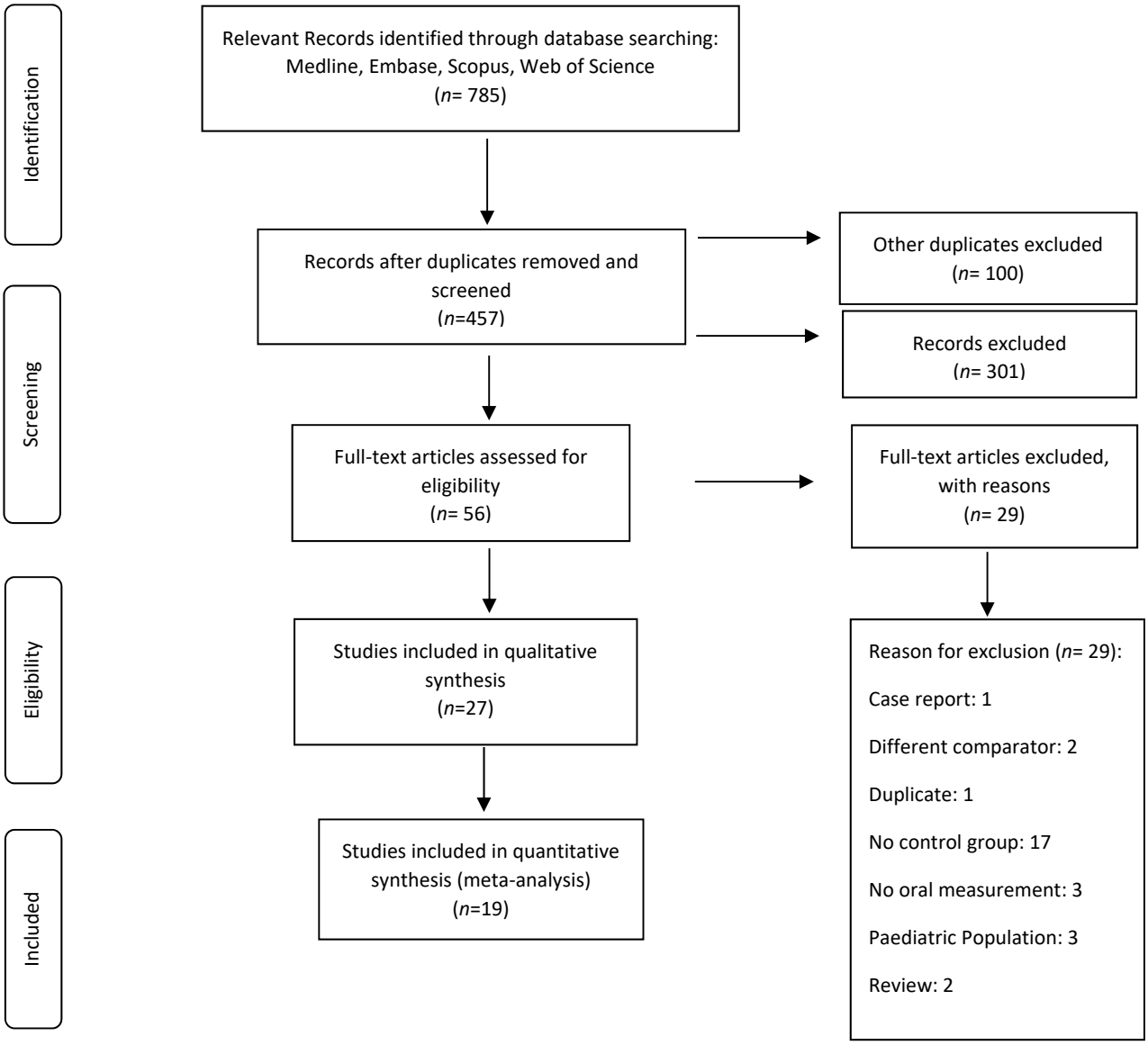
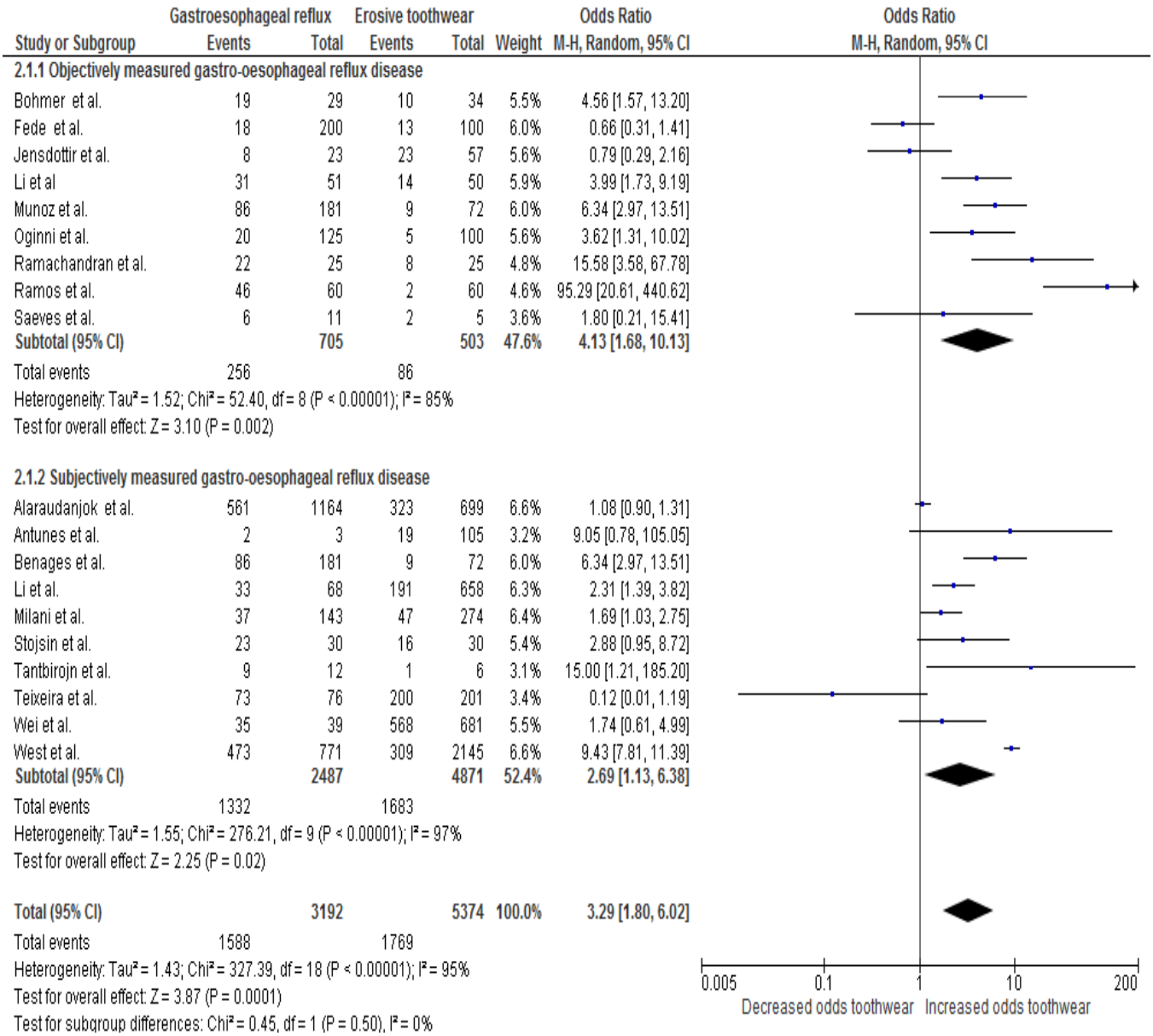


Figure 2. Forest plots illustrating meta-analyses of the odds of erosive toothwear in patients with objectively and subjectively measured gastro-oesophageal reflux disease/symptoms.



Appendix A. Supplementary data.

Supplementary table 1. Summary information of the inclusion criteria, search terms, study search filters and search dates for this systematic review of erosive toothwear in patients with gastro-oesophageal reflux disease/symptoms.

Inclusion Criteria	Population	Adults
	Intervention/exposure	*Dental assessment or self-reported dental symptoms with erosive toothwear *Endoscopic assessment or self-reported diagnosis of gastro-oesophageal reflux symptoms or related disease (GERD/S)
	Comparison	Individuals with GERD/S were compared with individuals without GERD/S.
	Outcome	Risk of erosive toothwear in individuals with GERD/S.
	Types of study	Cross-sectional, case-control, cohort, and/or intervention studies
Exclusion criteria		*Children (please note in our protocol this was defined as aged under 18 years, we subsequently relaxed this to children aged under 15 years old) *Case reports *Studies based solely on individuals with eating disorders (for example, anorexia nervosa, bulimia nervosa or rumination)
Information sources	Electronic databases	Ovid MEDLINE, Scopus, Embase, and Web of Science databases.
Search terms	1.Erosive toothwear	Tooth abrasion OR tooth attrition OR tooth erosion OR dentin sensitivity OR tooth wear OR toothwear OR crown lengthening.
	2.Gastro-oesophageal reflux disease	Reflux OR heartburn OR acid reflux* OR gastro-oesophageal reflux disease OR gastroesophageal reflux disease OR Barrett*? oesophagus* OR ?esophageal neoplasm OR (?esophag* adj5 (cancer* or adenocarcinoma*)).
	* Combination of 1 AND 2	
Filters	Language	English
	Species	Human
Search dates	From 1980 to 15/05/2018	Final confirmatory online search was done on 02/08/2019

Supplementary table 2: A summary of the different methods applied within studies to assess erosive toothwear.

Grade	**The index of Basic Erosive Wear Examination (BEWE)** (16,53,54)	
0	No toothwear.	
1	Initial loss of surface texture.	
2	Distinct defect, hard tissue loss <50% of the surface area.	
3	Hard tissue loss ≥50% of the surface area.	
Grade	**The index of Eccles and Jenkins** (17)	
0	No erosion.	
1	Loss surface details, change confined to enamel.	
2	Exposure of dentin affecting less than one-third of the crown.	
3	Exposure of dentin affecting one-third or more of the crown.	
Grade	**The index of Smith and Knight** (18)	
	Description the erosion according to anatomical location.	
0	No wear.	
1	Loss of enamel affecting less than 10% of the scored surface area.	
2	Enamel loss affecting less between 10% and one-third of the surface.	
3	Enamel loss affecting at least one-third but less than two-thirds.	
4	Enamel loss affecting less between 10% and two-thirds or more and no dentin exposure.	
5	Loss of dentin affecting less than one-third of dentin thickness.	
6	Dentin loss affecting between one-third and two-thirds of thickness on the scored surface.	
7	Dentin loss affecting two-thirds or more, with visible secondary dentin around the pulp chamber.	
Grade	**Visual erosion dental examination** (19)	
0	No erosive wear.	
1	Loss of enamel surface characteristic.	
2	Loss of enamel surface contour.	
3	Loss of dentine from less than one-third of the surface.	
4	Loss of dentine from more than and less than two-thirds of the surface.	
5	Loss of dentine from more than two-thirds of the surface	
Grade	**The index of Lussi** (20,31)	
	Criteria for anterior teeth	**Criteria for posterior teeth**
0	No evidence of erosion.	No evidence of erosion.
1	Loss of surface enamel, dentine not involved.	Enamel erosion of fissure system or cusps that cannot be attributed to the attrition, amalgam restoration stands proud above the enamel surface.
2	Erosion extending into dentine in at least one tooth.	Erosion into dentine that cannot be attributed to attrition, especially palatal aspects of maxillary molar cusps and buccal aspects of mandibular molar cusps.
3	Severe dentine erosion in at least four anterior teeth and or pulp chamber visible.	Erosion extending close to the pulp.

Supplementary table 3. Sensitivity and subgroup analyses of all studies investigating gastro-oesophageal reflux disease/symptoms and erosive toothwear combined, and by geographic location.

Studies(references)	Number of studies	Pooled risk estimate (95% CI)	I-squared (%)	p-value
All studies	n=19	3.29 (1.80-6.09)	95%	<0.001
Excluding individual studies				
Excluding Alaraud. Study (16)	n=18	3.54 (2.04-6.14)	88%	<0.001
Excluding Antunes study (34)	n=18	3.19 (1.72-5.89)	95%	<0.001
Excluding Benages study (35)	n=18	3.16 (1.68-5.94)	95%	<0.001
Excluding Bohmer study (53)	n=18	3.23 (1.74-6.05)	95%	<0.001
Excluding Fede study (30)	n=18	3.65 (1.96-7.78)	95%	<0.001
Excluding Jensdottir study (31)	n=18	3.58 (1.92-6.68)	95%	<0.001
Excluding Li study (24)	n=18	3.26 (1.73-6.13)	95%	<0.001
Excluding Li study (40)	n=18	3.38 (1.77-6.46)	95%	<0.001
Excluding Milani study (36)	n=18	3.45 (1.81-6.58)	95%	<0.001
Excluding Munoz study (12)	n=18	3.16 (1.68-5.94)	95%	<0.001
Excluding Ogini study (26)	n=18	3.28 (1.75-6.14)	95%	<0.001
Excluding Ramach. Study (29)	n=18	3.05 (1.64-5.66)	95%	<0.001
Excluding Ramos study (27)	n=18	3.05 (1.64-5.66)	94%	<0.001
Excluding Saeves study (19)	n=18	3.37 (1.82-6.25)	95%	<0.001
Excluding Stojsin study (39)	n=18	3.32 (1.77-6.21)	95%	<0.001
Excluding Tantbir. Study (37)	n=18	3.14 (1.70-5.80)	95%	<0.001
Excluding Teixeira study (17)	n=18	3.70 (2.01-6.80)	95%	<0.001
Excluding Wei study (6)	n=18	3.42 (1.83-6.40)	95%	<0.001
Excluding West study (32)	n=18	2.96 (1.82-4.83)	85%	<0.001
By geographic location				
European studies (11,12,16,17,19,30–32,35,39)	n=10	2.14 (0.86-5.32)	97%	<0.001
American studies (27,34,36,37)	n=4	11.52 (1.06-125.50)	90%	<0.001
Asian studies (16,24,29,40)	n=4	3.34 (1.67-6.68)	59%	0.06
African studies (26)	n=1	3.62 (1.31-10.02)	NA	0.01

Figure 3. Funnel plot assessing publication bias in 19 studies assessing the odds of erosive toothwear in patients with gastro-oesophageal reflux disease/symptoms.

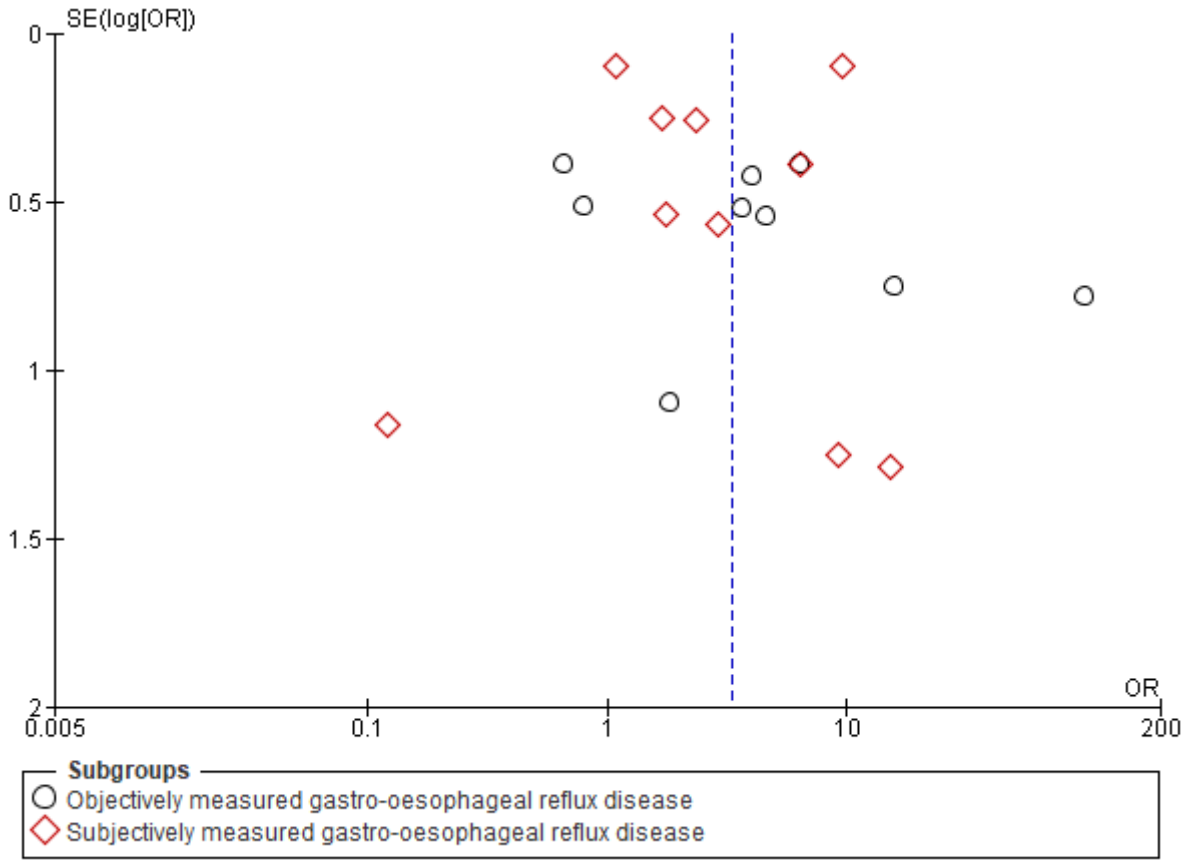


Figure3 legend: OR: Odds ratio; SE (log [OR]): the standard error of the log odds ratio.