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REVIEW ARTICLE

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Primary prevention of dental erosion by calcium and fluoride: a systematic review

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Abstract: *Background:* Overviews of the current literature only provide summaries of existing relevant preventive strategies for dental erosion. *Objectives:* To perform a systematic review according to the quantitative meta-analysis method of the scientific literature on prevention of dental erosion. The focused question will address primary prevention of dental erosion by calcium and fluoride. *Materials and methods:* Randomized clinical trials (RCTs) regarding dental erosion prevention. The search included five databases: Embase, Cochrane database of systematic reviews, PubMed (MEDLINE), FDA publication and Berman medical library of the Hebrew University. The search included data in the English language, with effect on preventing dental erosion always presented as mean enamel loss and measured by profilometer. Statistical meta-analysis was performed by StatsDirect program and PEPI statistical software. Fixed- and random-effect models were used to analyse the data. Heterogeneity tests were employed to validate the fixed-effect model assumption. *Results:* A total of 475 articles on dental erosion prevention were located. A four-stage selection process was employed, and 10 RCT articles were found to be suitable for meta-analysis. *Conclusions:* The number of studies on prevention of dental erosion maintaining standards of evidence-based dentistry remains insufficient to reach any definite conclusions. The focused questions of this review cannot be addressed according to the existing literature.

Key words: calcium; dental erosion; fluoride; prevention; systematic review

Introduction

Over a lifetime, teeth are exposed to a number of physical and chemical insults, which to various extents contribute to the wear and tear of dental hard tissues (1, 2) . Erosive tooth wear is defined as dissolution of tooth tissue by acids when the surrounding aqueous phase is undersaturated with appropriate minerals. In its broader definition, dental erosion is the irreversible loss of dental hard tissue due to a chemical process of acid dissolution but not involving bacterial plaque acid and not directly associated with mechanical or traumatic factors or with dental caries (1–3).

For many years, dental erosion has been a condition of little interest to clinical dental practice or dental public health. Prevalence data now show that erosive tooth wear is a common condition, among children and adults, with primary and permanent teeth similarly involved (3). As the population ages and teeth are increasingly retained for life, the incidence of dental erosion has escalated, demanding more appropriate preventive and restorative skills from the dental profession (4, 5).

Early diagnosis of dental erosion is important but difficult. No simple and valid diagnostic method has been devised, and defects are only detected clinically (1, 4, 6–9).

Dental clinicians often ignore or overlook the very early stages of erosion, dismissing minor tooth surface loss as a normal and inevitable occurrence of daily life. Thus, early diagnosis and consequent intervention are seldom reached (3, 8, 9). A survey in the UK has shown that only one third of the dental practitioners noted erosion on a frequent basis and the majority underestimated the prevalence of the condition (6). To increase the awareness of tooth erosion and to provide a guide to its clinical management, a new index system has recently been developed (6).

Existing overviews of the current literature on preventing dental erosion only summarize the potentially available preventive strategies. Increased acid resistance of dental hard tissues by fluoride therapy and increased resistance to hydroxyapatite dissolution by provision of calcium have been found to be effective (10).

Systematic reviews and meta-analysis are considered important instruments for evaluation of medical treatments, utilizing a structured approach in retrieving, analysing and interpreting the evidence (11–13).

The purpose of this systematic review was to review and critically appraise, by the method of quantitative meta-analysis, the scientific literature regarding the efficacy of primary prevention by calcium and fluoride of dental erosion, by comparing *in vivo* and *in situ* high and low erosive ingredients, and to harmonize a discordant literature by a statistical method of combining the results of multiple studies.

Materials and methods

Focused PICO question

In adults, what is the efficacy of calcium and fluoride on preventing dental erosion, by comparing *in vivo* and *in situ* high and low erosive ingredients?

Data

This systematic review includes randomized clinical trials (RCTs) of dental erosion prevention. The protocol included guidelines for the literature search, study quality considerations, patients' inclusion criteria, outcome parameters and statistical methods to be used in the meta-analysis. The used search terms and the combination are described in Fig. 1. The focused question will address primary prevention of dental erosion by calcium and fluoride.

Sources

The search was conducted in five databases:

- Electronic search of PubMed (MEDLINE);
- Electronic search of Cochrane database of systematic review;
- Electronic search of Embase;
- Electronic search of FDA publications;
- Manual search Berman medical library, Hebrew University, Jerusalem.

Search terms used for PubMed (Medline), Cochrane Database of Systematic Review, Embase, FDA publications, and Berman medical library, Hebrew University, Jerusalem.

The search strategy was customized according to each database that was searched.

The following terms were used in the search strategy:

"dental erosion prevention clinical trials"; "dental erosion prevention case report"; "dental erosion AND prevention trials"; "dental erosion AND prevention cohort studies"; "dental erosion AND prevention studies"; "dental erosion AND prevention clinical"; "dental erosion AND prevention"; "dental erosion AND preventive epidemiological trials"; "erosive tooth wear AND prevention"; "dental erosion AND prevention AND systematic review", dental erosion AND calcium" "dental erosion AND fluoride".

Fig. 1. Sources search strategy and items.

Search strategy

A four-stage selection process was employed according to the protocol criteria and presented in Fig. 2. Reproducible search strategy was used to reduce bias by repeated search and analysis after 4–6 weeks by the same researcher (K.Y.) and a different search and analysis by a colleague (A.Z.). The period of research selection was not limited and was done during 2011.

Statistical methods used in meta-analysis

Sample size and event rate justify the use of a weighted mean difference. The weighted mean difference expresses the

Primary selection

- Randomized control trials (RCTs)
- English language (difficulties to obtain a reliable translation of non-English papers)
- Relevant to dental erosion prevention

Secondary selection

- Specific preventive substances (calcium and fluoride)

Tertiary selection

- Study type: RCTs *in vivo* and *in situ* studies
- Sample type: deciduous or permanent enamel samples

Quartile selection

- Studies with appropriate statistical data that is suitable for an analysis
- Studies with appropriate statistical data that is suitable for an analysis

Fig. 2. Selection search strategy.

weighted size of the intervention effect by the individual variances for each study.

Meta-analysis provides a summary estimate by weighting each study effect in inverse proportion to its variance. The inverse variance method is based on fixed- and random-effect models and assumes that there is a constant true mean effect size around which the true value being a random sample error. This was tested by homogeneity statistics.

Effect size is a statistical measure for the magnitude of difference between interventions adjusted by estimate of variability that is suitable for dichotomous and continuous data. It is calculated for each article or study and for each outcome parameter. The results of the meta-analysis were analysed using StatsDirect statistical software, version 2.7.7 (StatsDirect Ltd, Cheshire, UK) and Module I of compare2, version 2.34 of the software pepi (14).

Presentation of the results

The results are presented in graphs, funnel plots and forest plots. Statistical terms included difference, strata and confidence interval. Bias was assessed by two bias indicators: Begg–Mazumdar using Kendall's tau for testing the interdependence of variance and effect size and Egger for asymmetry of the funnel plot. Heterogeneity test for comparison of strata and Cochran Q measured for studying whether effects of different studies are around the same true mean effect were used. In case of a P-value<0.1, data were analysed using fixed- and random-effect models. Consistency of handling the data and combining results was assessed by I^2.

In our study, both random- and fixed-effects models were used, due to the fact that each entails a series of assumptions that might be violated in any given data set. Under certain conditions, random-effect model can introduce bias but reduce the variance of estimates of coefficients of interest, while fixed effect will be unbiased but may be subject to high variance.

Random-effect model was additionally used due to the fact that we know that the effect sizes might differ and to highlight how the underlying model affects the results.

The funnel plot is a graphic method designed to check bias in meta-analysis. A symmetric inverted shape indicates a low bias, while an asymmetric plot indicates a relationship between treatment effect and study size. As mentioned, existence of publication and selection bias was checked by bias indicator statistical tests. Cases in which P-value <0.01 indicate a possible bias.

The forest plot is a graphic method in which for each study the effect size and the corresponding confidence interval (95%) are presented (12). Small studies will present a large range of confidence intervals, and large studies will present a small range of confidence intervals.

Grading the 'body of evidence'

We utilized the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system, as proposed by the GRADE working group (15, 16). Two reviewers (ZA and VY) rated the quality of the evidence according to the following aspects: type of evidence (all RCTs), quality points, consistency, directness and effect size.

Results

As presented in Fig. 3, a total of 475 articles on dental erosion prevention were found. Following the selection process, 19 articles were approved by the primary selection. Of those, three articles did not involve calcium or fluoride, three did not follow study and sample compatibility and another three demonstrated inappropriate statistical data. Finally, only 10 RCT *in situ* studies of two substance groups, calcium and fluoride, were suitable for meta-analysis. These were all presented as mean enamel loss and measured by profilometer.

The characteristics of the trials are highlighted in Table 1a (calcium group A) and Table 1b (fluoride group B).

The calcium trial group included six articles (Table 1a):

The first article (17) evaluated a low erosive blackcurrant juice and calcium concentrate drink in comparison with orange juice. The second article (18) evaluated a concentrate drink of a low erosive blackcurrant juice and calcium drink in comparison with other low pH fruit drinks. The third article (19) evaluated a low erosive blackcurrant juice and calcium concentrate drink in comparison with conventional blackcurrant juice drink and orange juice. The fourth article (20) evaluated further modification of a low erosive blackcurrant juice and calcium concentrate drink by the addition of a xanthan gum. The fifth article (21) evaluated a modification of a low erosive blackcurrant juice and calcium concentrate drink with xanthan gum to minimize erosion. The sixth article (22) assessed the erosive effect of acidic soft drinks containing food-approved polymers in comparison with unmodified soft acidic drinks.

The fluoride trial group included four articles (Table 1b):

The first article (23) evaluated the effect of fluoride dentifrice on eroded enamel subjected to brushing abrasion. The second article (24) evaluated the effect of fluoride varnish in the prevention of wear due to erosion. The third article (25) evaluated the protective effects of experimental fluoride-based toothpastes against dental erosion. The fourth article (26) evaluated the salivary residual effect of fluoride dentifrice on enamel erosion.

The statistical data of the 10 selected articles for meta-analysis on dental erosion prevention are presented in Table 2. Heterogeneity test Cochran Q (Table 3) for calcium studies (28.94; d.f. = 5; $P < 0.0001$) and for fluoride studies (26.67; d.f. = 3; $P < 0.0001$) demonstrated statistically significant results. In performing 2 tests of 'bias indicators', both groups yield statistically significant results ($P = 0.006$ and $P = 0.013$, respectively), indicative of a possible publication bias.

Figure S1a presents a relatively symmetrical distribution of 6 studies in group A (three positive and three negative), but not an inverted funnel plot. Similarly, Figure S1b presents a relatively symmetrical distribution of group B (two positive and two negative), but not an inverted funnel plot. These results indicate a possible publication or selection bias.

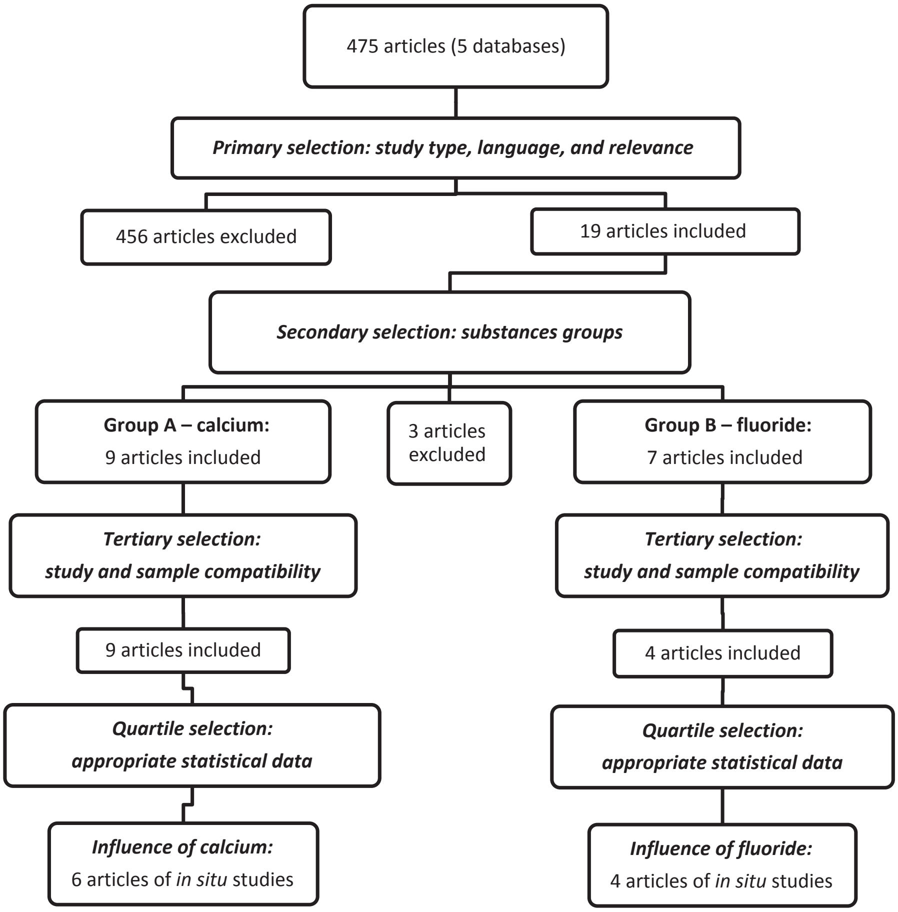

Fig. 3. Flow chart of the four-stage selection process.

The results of the meta-analysis of each group are presented in Fig. 4a and b. According to Fig. 4a, the protective calcium pooled means of the fixed-effect (FE) model and the random-effect (RE) model (−0.12 and −0.25, respectively) were not statistically significant. According to Fig. 4b, the protective fluoride pooled means of the fixed-effect model and the random-effect model (−0.41 and −0.75, respectively) were also not statistically significant.

The GRADE evidence profile for the primary prevention of dental erosion by calcium and fluoride is presented in Table 4. Based on the scoring system for clinical evidence reviews, the final GRADE score was very low.

Discussion

The two main goals of evidence-based dentistry are to supply the best evidence and consecutively to transfer practical applications (27). The purpose of the present study was to perform a systematic review by quantitative meta-analysis of the existing scientific literature on prevention of dental erosion.

Of 475 articles, the four-stage selection process identified 10 *in situ* studies suitable for final analysis: six articles examined the influence of calcium (as food or drink additive) for prevention of dental erosion, and four articles examined the influence of fluoride on prevention of dental erosion. The effect on dental erosion was examined by means of profilometric measurement of enamel loss in response to the substance in comparison with a control group in which water was the golden standard.

The funnel plots (Figure S1a and b) of the calcium and fluoride studies regarding dental erosion prevention had no inverted shape, which is indicative of a non-ideal scattering of studies around the overall mean effect. The fact that, nevertheless, the result had a symmetrical distribution of positive and negative studies leads to the assumption that the amount of studies of dental erosion prevention suitable for meta-analysis is not sufficient. In both groups, a significant heterogeneity was found, which might be due to the small numbers of studies, a small sample size in each study or a possible indication of publication bias. In addition, the performance of two tests of 'bias indicators' (Table 3) demonstrated a possible selection bias. It should be noted that the power of Egger method to detect bias might be low with small numbers of studies.

With regard to the forest plots of the calcium and fluoride studies (Fig. 4a and b), in the six studies of calcium and its influence on loss of enamel, the pooled mean effect size was protective, guided by two studies with statistically significant effect (17–19), but with no overall statistical significance. In

Table 1. **(a) Characteristics of the six *in situ* trials (group A – influence of calcium) included in the meta-analysis of dental erosion prevention. (b) Characteristics of the four *in situ* trials (group B – influence of fluoride) included in the meta-analysis of dental erosion prevention**

(a)

Trial	Objective	Design	*n*	Duration	Adverse effects	Clinical implications
Hughes *et al.* (17)	To compare low erosive blackcurrant juice and calcium concentrate drink with orange juice	Single-centre, single-blind, randomized placebo-controlled 3-cell crossover	12	15 days	None	Blackcurrant juice drink with calcium is markedly less erosive to teeth than orange juice
Hughes *et al.* (18)	To demonstrate that a blackcurrant juice drink with added calcium produced little erosion as compared to other low pH fruit drinks	Single-centre, single-blind, randomized placebo-controlled 5-cell crossover	15	15 days	None	Consumption of blackcurrant juice drink with added calcium would take in excess of 100 years as compared to periods ranging from as little as 2 years to 20 years in consumption of standard low pH fruit drinks, regarding 1 mm erosive loss of enamel
West *et al.* (19)	To compare low erosive blackcurrant juice and calcium concentrate drink with conventional blackcurrant juice drink and orange juice	Single-centre, single-blind, randomized placebo-controlled 4-cell crossover	12	15 days	None	The very low comparative erosivity of the further modified blackcurrant juice drink with calcium supports the development of such drinks for public consumption
Hughes *et al.* (20)	To further modify an original low erosive blackcurrant juice and calcium concentrate drink by the addition of a xanthan gum to manipulate more favourably other drink parameters	Single-centre, single-blind, randomized 4-treatment crossover	12	10 days	None	Modification of blackcurrant drinks through the addition of xanthan gum allowed adjustment to the product without influencing enamel erosion to any clinically significant extent
West *et al.* (21)	To compare the erosive effect of a low erosive blackcurrant juice and calcium concentrate drink with xanthan gum with a low erosive product	Single-centre, single-blind, randomized 4-treatment crossover	16	15 days	None	The new blackcurrant and calcium and gum added drink caused significantly less enamel loss than conventional blackcurrant drink
Hooper *et al.* (22)	To determine the erosive effect of acidic soft drinks containing food-approved polymers with the erosive effect of unmodified soft acidic drinks	Single-centre, single-blind, randomized 5-treatment crossover	15	10 days	None	Unmodified acidic soft drinks with the addition of polyphosphate alone or combined with calcium or xanthan gums are all effective at reducing erosion of enamel compared with the unmodified soft acidic drink

(b)

Magalhães *et al.* (23)	To evaluate the effect of fluoride dentifrice on eroded enamel subjected to brushing abrasion	Single-centre, double-blind, randomized crossover	10	14 days	None	Fluoride dentifrice has a protective effect on eroded enamel subjected to brushing abrasion
Vieira *et al.* (24)	To evaluate the inhibition of erosive tooth wear by fluoride varnish	Single centre, single blind, randomized	11	21 days	None	Fluoride varnish is effective in the reduction in erosive tooth wear
Hooper *et al.* (25)	To evaluate the protective effect of experimental fluoride-based toothpaste against erosion	Single-centre, single-blind, randomized, three-way crossover	15	15 days	None	The sodium hexametaphosphate toothpaste causes less erosive damage as compared to the fluoride control toothpaste
Magalhães *et al.* (26)	To evaluate the influence of residual salivary fluoride from dentifrice on enamel erosion	Single-centre, double-blind, randomized crossover	10	14 days	None	Residual salivary fluoride from dentifrice does not present a preventive effect against dental erosion

Table 2. **Statistical data of the 10 selected articles for meta-analysis of dental erosion prevention**

Article	g	Exact 95% CI		*n* (experimental)	*n* (control)	d	Approximate 95% CI		Test for heterogeneity χ^2	*P*
Group A of 6 *in situ* studies – influence of calcium versus water										
Hughes *et al.* (17)	0.965	−0.370	1.252	12	12	0.430	−0.379	1.240	24.46	<0.001
Hughes *et al.* (18)	0.965	−2.989	−1.000	15	15	−1.939	−2.909	−0.969	27.35	<0.001
West *et al.* (19)	0.965	−1.845	−0.141	12	12	−0.968	−1.814	−0.122	14.18	<0.001
Hughes *et al.* (20)	0.965	−1.333	0.297	12	12	−0.506	−1.319	0.306	23.13	<0.001
West *et al.* (21)	0.973	0.005	1.488	16	16	0.732	−0.007	1.472	28.21	<0.001
Hooper *et al.* (22)	0.973	−0.113	1.356	15	15	0.610	−0.122	1.342	24.71	<0.001
Group B of 4 *in situ* studies – influence of fluoride versus water										
Magalhães *et al.* (23)	−0.982	−1.902	−0.038	10	10	−0.940	−1.864	−0.017	23.96	<0.001
Vieira *et al.* (24)	−2.989	−4.215	−1.729	11	11	−2.876	−4.067	−1.684	7.71	0.021
Hooper *et al.* (25)	0.696	−0.047	1.429	15	15	0.678	−0.058	1.413	13.56	0.001
Magalhães *et al.* (26)	−0.071	−0.948	0.807	10	10	−0.068	−0.945	0.808	25.63	<0.001

Table 3. **Meta-analysis tests results of studies on prevention of dental erosion**

	Fixed effects (Hedges–Olkin)			Non-combinability of studies				Bias indicators: Begg–Mazumdar		Egger	
	d+* (95% CI[†])	Z[‡]	*P*	Cochran Q	d.f.	*P*	I² % (95% CI[†])	Kendall's tau	*P*	Bias	*P*
Group A – calcium	−0.11 (−0.44, 0.22)	−0.68	0.499	28.94	5	<0.001	82.7 (57.4, 90.3)	−0.87	0.003	−22.70	0.006
Group B – fluoride	−0.59 (−1.25, 0.08)	−1.72	0.086	26.67	3	<0.001	88.8 (70.0, 93.9)	−1.00	<0.001	−15.45	0.013

*Pooled effect size.
[†]Confidence interval.
[‡]Z test d+ differs from 0.

the four studies of fluoride and its influence on loss of enamel, the pooled mean effect size was protective, guided by two studies with statistically significant effect (23, 24), but with no overall statistical significance.

It is important to note that water was the gold standard substance in all of the studies, causing almost no erosion. The fact that the effect of calcium and fluoride was found not to be significant when compared to the effect of water does not imply that these substances have no potential clinical effect, only that the pooled research data did not achieve clearly convincing statistical significance. Also, the final categorization of evidence based on the GRADE score in the present study does not necessarily relate to the overall methodological quality of any individual RCT.

It is interesting to note that the *in situ* studies indicated that fluoride may be to some extent more effective than calcium. It is generally accepted that systematic reviews and randomized controlled trials represent the best level of evidence (27, 28). However, studies at an optimal level are difficult to execute due to barriers such as cost, difficulty to maintain blindness, inclusion criteria and ethical problems (27). In fact and unfortunately, several methodologies have been introduced to the clinical milieu without randomized controlled trials (27).

The strengths and limitations of the meta-analysis method have been discussed (28, 29). Authors have a wide range of different backgrounds and research methodology understanding, and this often leads to lack of sufficiently valid data and extensive exclusion of studies from the meta-analysis. It should be noted that we used only English written studies due to the reason that it is not always possible to obtain a reliable translation of these papers. Negative studies are more likely to be published in local than in international journals, and therefore, it might exclude negative studies from the analysis (30).

Conclusions

The number of studies on prevention of dental erosion achieving the standards of evidence-based dentistry is not adequately sufficient to reach any irrefutable conclusions after employing meta-analysis. Therefore, the focused questions of this review cannot be addressed according to the current literature. The insufficient data highlighted in our study might serve as a benchmark for a need of further research on dental erosion prevention. To establish a solid base of evidence-based dentistry, there is a need to perform randomized blind clinical

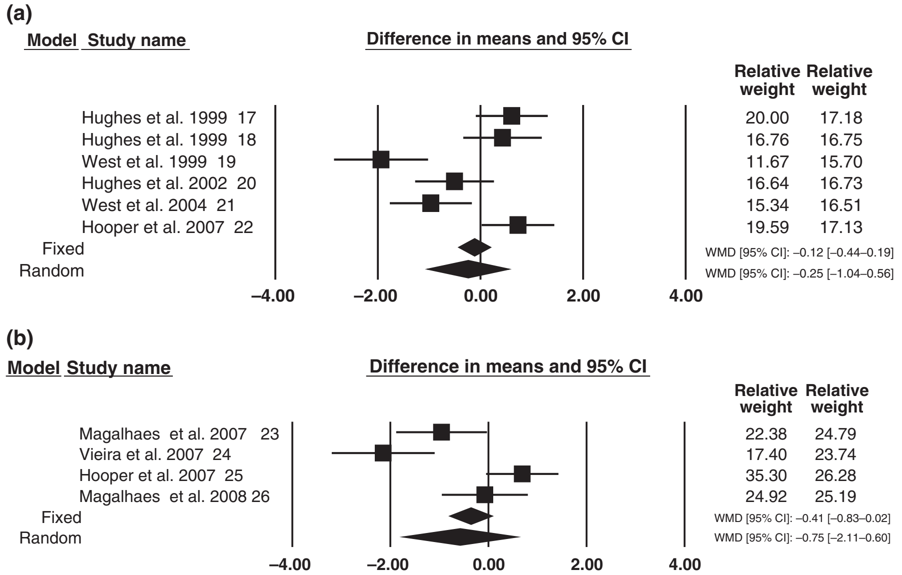

Fig. 4. (a) Meta-analysis forest plots of calcium studies of prevention of dental erosion. (b) Meta-analysis forest plots of fluoride studies of prevention of dental erosion.

Table 4. **GRADE evidence profile for the impact of the use of calcium and fluoride in primary prevention of dental erosion**

	Calcium	Fluoride
Quality	High	High
Consistency	Inconsistent	Inconsistent
Directness	Not generalizable	Not generalizable
Effect size	Not statistically significant	Not statistically significant
Strength of recommendations	Very low	Very low

trials. These studies should also include preventive substances other than calcium and fluoride and should encompass larger and more compatible study samples. Optimal research will serve as the foundation supporting the dental clinician with providing the best quality of care for the patient.

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Supporting information

Additional supporting information may be found in the online version of this article.

Figure S1. (a) Meta-analysis funnel plots of calcium studies of prevention of dental erosion. (b) Meta-analysis funnel plots of fluoride studies of prevention of dental erosion.