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SCIENTIFIC SECTION

Fluorides, orthodontics and demineralization: a systematic review

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Objectives: To evaluate the effectiveness of fluoride in preventing white spot lesion (WSL) demineralization during orthodontic treatment and compare all modes of fluoride delivery.

Data sources: The search strategy for the review was carried out according to the standard Cochrane systematic review methodology. The following databases were searched for RCTs or CCTs: Cochrane Clinical Trials Register, Cochrane Oral Health Group Specialized Trials Register, MEDLINE and EMBASE. Inclusion and exclusion criteria were applied when considering studies to be included. Authors of trials were contacted for further data.

Data selection: The primary outcome of the review was the presence or absence of WSL by patient at the end of treatment. Secondary outcomes included any quantitative assessment of enamel mineral loss or lesion depth.

Data extraction: Six reviewers independently, in duplicate, extracted data, including an assessment of the methodological quality of each trial.

Data synthesis: Fifteen trials provided data for this review, although none fulfilled all the methodological quality assessment criteria. One study found that a daily NaF mouthrinse reduced the severity of demineralization surrounding an orthodontic appliance (lesion depth difference –70.0 μm; 95% CI –118.2 to –21.8 μm). One study found that use of a glass ionomer cement (GIC) for bracket bonding reduced the prevalence of WSL (Peto OR 0.35; 95% CI 0.15–0.84) compared with a composite resin. None of the studies fulfilled all of the methodological quality assessment criteria.

Conclusions: There is some evidence that the use of a daily NaF mouthrinse or a GIC for bonding brackets might reduce the occurrence and severity of WSL during orthodontic treatment. More high quality, clinical research is required into the different modes of delivering fluoride to the orthodontic patient.

Key words: Systematic review, compomer, demineralization, fluoride, glass ionomer, orthodontic

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Introduction

White spot lesion (WSL) demineralization is a significant problem during orthodontic treatment. One cross-sectional study[1] found that 50% of individuals undergoing brace treatment had a non-developmental WSL compared with 25% of controls. Another study[2] found that, even 5 years after treatment, orthodontic patients had a significantly higher incidence of WSLs than a control group of patients who had not had orthodontic treatment.

Fluoride is important in the prevention of enamel demineralization.[3] There are several methods of delivering fluoride to teeth in patients during orthodontic treatment (in addition to fluoridated toothpaste). These include:

- topical fluorides (e.g. mouthrinse, gel, varnish, toothpaste);
- fluoride-releasing materials (e.g. bonding materials, elastics).

A recent systematic review[4] has found a reduced level of caries in children and adolescents who have regular

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supervised rinsing with a fluoride mouthwash. The primary objective of this review was to evaluate the effectiveness of fluoride in preventing the occurrence of WSL on the teeth during orthodontic treatment. The secondary objective was to examine the effectiveness of the different modes of delivery.

The following null hypotheses were considered:

- There is no difference in the incidence of WSL between patients undergoing fixed orthodontic treatment who receive fluoride and those that do not.
- There is no difference in the incidence of WSL between patients undergoing fixed orthodontic treatment who receive fluoride in the different ways.

Methods

The method for this review is presented according to Cochrane guidelines with the help of the Cochrane Oral Health Group.[5]

Types of studies considered in the review

Randomized (RCT) or quasi-randomized controlled clinical trials (CCT) in which fluoride is delivered by any method, to prevent enamel WSL formation during orthodontic treatment.

Types of participants

Patients of any age undergoing orthodontic treatment with fixed appliances.

Types of interventions

- Topical fluoride in the form of toothpaste, mouthrinse, gel and varnish at any dose, frequency, duration or method of administration, and with any of the following active agents/ingredients: NaF (sodium fluoride), SMFP (sodium monofluorophosphate), SnF (stannous fluoride), APF (acidulated phosphate fluoride), amine F (amine fluoride).
- Materials containing fluoride that is released during treatment including: fluoride-releasing composite resin bonding materials, glass ionomer cements (GIC), compomers and resin-modified GICs for bonding or banding, slow release fluoride devices, fluoride-releasing elastomeric ligatures.
- The control group was either individuals or teeth within the same individual (including the split-mouth technique for application of fluoride via bonding or cementing agents and ligatures) not subjected to the fluoride intervention, either through a placebo, such as a non-fluoride toothpaste and mouthrinse, or absence of the intervention. Studies involving a control subjected to an alternative fluoride intervention were also included.

Types of outcome measures

For parallel group studies the primary outcome measure was the presence/absence of new WSL by the patient at the end of treatment. If the number of WSL was not recorded at the start of treatment then the outcome was the presence or absence of WSL at the end of treatment. For split-mouth studies a cross-tabulation by treatment was calculated showing presence/absence of WSL per quadrant.

Secondary outcomes included differences in size and severity of WSL between experimental and control groups, and any quantitative assessment of enamel mineral loss, either directly using contact microradiography or indirectly using techniques such as enamel hardness testing. Also included were any patient-based outcomes, such as perception of WSL and quality of life data.

Search strategy for identification of studies

The search strategy for the review was carried out according to the standard Cochrane systematic review methodology. The following databases were searched for randomized or quasi-randomized clinical trials:

- Cochrane Clinical Trials Register (January 2004);
- MEDLINE (1966 to December 2004);
- EMBASE (1974 to December 2004).

The search strategy used a combination of controlled vocabulary and free text terms such as orthodontics, cariostatic agents, fluorides-topical, glass ionomer cements, dental enamel solubility and tooth demineralization.

Search Strategy

Fluorides, Orthodontics and Demineralization: A Systematic Review

1. exp ORTHODONTICS/
2. orthodontic$.mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
3. 1 or 2
4. exp Cariostatic Agents/
5. exp Fluorides, Topical/
6. fluoride$.mp. [mp=title, original title, abstract, name of substance, mesh subject heading]

7. (topical adj5 fluoride).mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
8. NaF.mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
9. exp Glass Ionomer Cements/
10. (glass adj5 ionomer$).mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
11. exp COMPOMERS/
12. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13. exp Dental Enamel Solubility/
14. exp Tooth Demineralization/
15. (demineral$ or remineral$ or decalcifi$).mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
16. (white adj5 spot$).mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
17. 13 or 14 or 15 or 16
18. 3 and 12 and 17
19. limit 18 to randomized controlled trial
20. limit 18 to controlled clinical trial
21. exp Randomized Controlled Trials/
22. exp Random Allocation/
23. exp Double-Blind Method/
24. exp Single-Blind Method/
25. 19 or 20 or 21 or 22 or 23 or 24
26. (animal not human).mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
27. 25 not 26
28. limit 18 to clinical trial
29. exp Clinical Trials/
30. (clin$ adj25 trial$).mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
31. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
32. exp PLACEBOS/
33. placebo$.mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
34. random$.mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
35. exp Research Design/ (189137)
36. 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35
37. 36 not 26
38. 37 not 27
39. Comparative Study/
40. exp Evaluation Studies/
41. exp Follow-Up Studies/
42. exp Prospective Studies/
43. (control$ or prospectiv$ or volunteer$).mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
44. 39 or 40 or 41 or 42 or 43
45. 44 not 26
46. 45 not (27 or 38)
47. 27 or 38 or 46
48. 18 and 47

The Cochrane Oral Health Group Specialized Trials Register (January 2004), which includes trials identified by hand searching dental journals, was also searched. The bibliographies of identified randomized controlled clinical trials (RCTs) and review articles were checked for studies outside the journals found. Personal references were also searched. Authors of the identified CCTs and RCTs were written to in an attempt to identify unpublished or ongoing studies, but no further studies were supplied and, therefore, publication bias is difficult to assess. No language restriction was applied.

Data extraction

Data were extracted and methodological quality assessed by two reviewers independently, in duplicate, using specially designed data extraction forms. The data extraction forms were piloted on several papers and modified as required before use. Any disagreement was discussed and a third reviewer consulted where necessary.

The four major quality criteria were:

- method of randomization;
- allocation concealment;
- blinding of outcome assessment;
- completeness of follow-up.

Other methodological criteria examined were: presence or absence of a sample size calculation, comparability of groups at the start, clear inclusion/exclusion criteria and presence/absence of an estimate of measurement error. Agreement between reviewers, concerning methodological quality, was assessed by calculating kappa values.

Data synthesis

A weighted treatment effect was calculated and the results expressed as weighted mean differences (WMD and 95% CI) for continuous outcomes and Peto odds ratio (OR and 95% CI) for dichotomous outcomes, using random effects models.[6] Data from included studies were derived from intra-individual (split-mouth) and parallel group studies. In order to combine continuous or dichotomous outcome variables from these different study design the use of the generic inverse variance procedure was planned.[7] However, due to the diverse methods, outcomes and assessments used in the included trials no meta-analyses, combining more than one study, were undertaken.

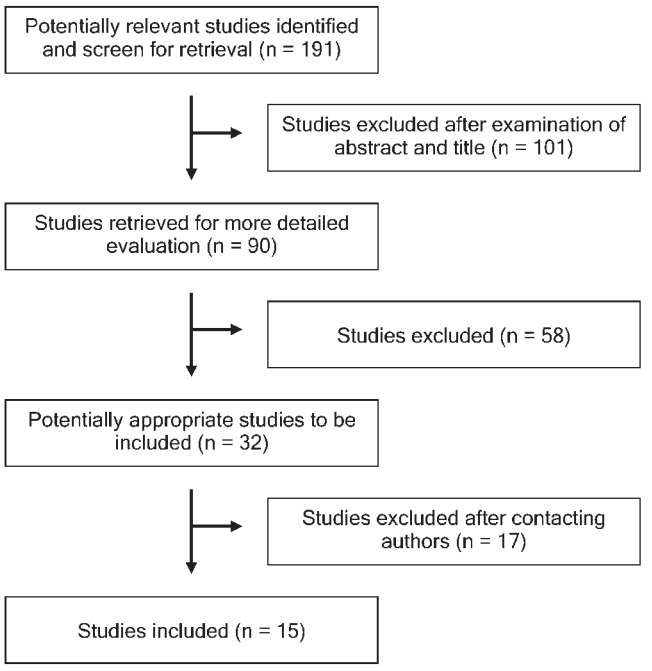

Figure 1 Flow diagram detailing studies screened during the review after Moher *et al.*[23]

Results

Description of studies

The description of studies examined is summarized in Figure 1. The searches identified 191 studies, of which 101 were excluded after reviewing the title or abstract. Full articles were obtained for the remaining 90. From the full articles, 58 studies proved ineligible. Of the remaining 32 studies, two reports were abstracts of trials more fully detailed in other publications and 18 authors were contacted for further information concerning 29 reports. Twelve of these studies were excluded, mainly because the authors were unable to provide further data and three are pending further information from the authors. Therefore, 15 studies from 14 publications, fulfilled all the criteria for inclusion. A summary of all the included trials is shown in Table 1.

The kappa scores and percentage agreements between the two raters assessing the major methodological quality of the studies were:

- randomization 0.56, 82%;
- concealment 0.62, 91%;
- blinding 1.00, 100%;
- withdrawals 0.64, 83%.

Comparison of fluoride products

Acid-phosphate-fluoride mouthrinse versus no mouthrinse. One trial[8] compared daily acid-phosphate-fluoride mouthrinse with a no mouthrinse regimen. This was a controlled clinical trial involving 60 patients treated with orthodontic fixed appliances (banded) aged 10–14 years. Participants were allocated alternately to either the experimental group (daily acid-phosphate-fluoride mouthrinse) or control (no mouthrinse). The outcome measure was the number of new WSL on the lateral incisors and first permanent molars. There was no statistically significant difference between the experimental and control groups in the proportion of patients with WSL, Peto OR 0.41 (95% CI 0.14–1.20). However, the risk of bias was judged high, because it failed to fulfill any of the major methodological criteria and we were unable to contact the original author of this paper to clarify the methodology.

Sodium fluoride mouthrinse versus no mouthrinse. One trial[9] compared two parallel groups of patients, each requiring the extraction of premolars as part of their orthodontic treatment to relieve crowding. Poorly fitting bands were placed on the premolars for 4 weeks, during which the experimental group rinsed daily with a neutral solution of 0.2% sodium fluoride and the control group received no fluoride supplementation. The outcomes were mineral loss and lesion depth, measured using contact microradiography on the enamel of the teeth after they had been extracted. The results showed no difference in mineral loss between the experimental and the control groups, but a significantly decreased lesion depth in the experimental group, although the standard deviation of the experimental group was nearly half that of the control group mean difference –70 μm (95% CI –118 to –22 μm). However, the study was judged to have a high risk of bias, as it failed to fulfill any of the major or minor methodological criteria.

MFP versus stannous fluoride mouthrinses. One clinical trial[10] compared two parallel groups who rinsed daily with either a 0.1% solution of stannous fluoride (experimental) or a 0.184% solution of sodium monofluorophosphate (control). The odds ratio for these results was not significant (Peto OR 0.10; 95% CI 0.01–1.72). The study was judged to have a high risk of bias as it failed to fulfill any of the major or minor criteria for methodological quality.

Fluoride and antimicrobial varnish versus fluoride varnish. One study[11] examined the differences between a group of patients treated with a combination of an antimicrobial varnish (Cervitec, 1% chlorhexidine, 1% thymol; Vivadent, Schaan, Liechtenstein) and a fluoride varnish (Fluor Protector, 5% difluorosilane; Vivadent), applied alternately at treatment visits (each varnish every 12 weeks) and a control group that received a placebo varnish (Cervitec without the chlorhexidine and thymol) instead of the antimicrobial varnish and the

Table 1 Summary of included clinical studies

Reference	Design	Participants	Outcomes	Quality assessment	Risk of bias
Acid-phosphate fluoride mouthrinse versus no mouthrinse					
Hirschfield[8]	CCT; 2 parallel groups; allocated alternately; treatment time 20–28 months	30 expt; 30 control. Age range 10 – 14 years	Number and severity of white spots assessed by clinical exam before and after treatment (modified Gorelick Index)	Randomisation – No Allocation concealment – No Assessor blinding – No Dropouts described – Unclear Sample justified – No Baseline comparison – Unclear Inclusion/Exclusion criteria – Yes Method error – No	High
Sodium fluoride mouthrinse versus no mouthrinse					
Ogaard *et al*[9]	RCT; parallel groups	10 patients (5 expt with 10 teeth, 5 control with 5 teeth) Age ranges: Control 8–13 years; Expt 11–13 years	Mineral loss and lesion depth on extracted premolars with contact microradiography performed	Randomisation – No Allocation concealment – No Assessor blinding – No Dropouts described – Unclear Sample justified – No Baseline comparison – Unclear Inclusion/Exclusion criteria – Yes Method error – No	High
Stannous fluoride versus MFP mouthrinse					
Dyer & Shannon[10]	CCT; 2 parallel groups; followed for 1 year	12 patients used SnF mouthrinse; 10 used MFP mouthrinse. Age range 11–15 years	Number of new white spots and severity, assessed by clinical exam	Randomisation – Unclear Allocation concealment – Unclear Assessor blinding – No Dropouts described – Unclear Sample justified – No Baseline comparison – Unclear Inclusion/Exclusion criteria – No Method error – No	High
Fluoride and antimicrobial varnish versus fluoride varnish					
Ogaard *et al*[11]	RCT; 2 parallel expt groups; historical untreated control	110 patients in each group Age range 12–15 years	Visual inspection of white spots	Randomisation – Yes Allocation concealment – Unclear Assessor blinding – No Dropouts described – Unclear Sample justified – No Baseline comparison – No Inclusion/Exclusion criteria – No Method error – No	High

Table 1 *(continue)*

Reference	Design	Participants	Outcomes	Quality assessment	Risk of bias
Fluoridated versus non-fluoridated composite for bonding					
Sonis & Snell[12]	CCT; split-mouth design	22 patients. Mean age 19 years, range 11 – 58 years	Number and severity of white spots, assessed from clinical exam orphotographic assessment after treatment	Randomisation – No Allocation concealment – No Assessor blinding – No Dropouts described – Yes Sample justified – No Baseline comparison – Unclear Inclusion/Exclusion criteria – No Method error – No	High
GIC versus composite for bonding					
Chung *et al*[15]	RCT; split-mouth design	13 patients Mean age 13.4 years (including Chung)	Number and severity of white spots - assessed with modified Gorelick Index from before and after treatment photographs by one blinded examiner	Randomisation – Yes Allocation concealment – Yes Assessor blinding – Yes Dropouts described – Yes Sample justified – No Baseline comparison – Unclear Inclusion/Exclusion criteria – No Method error – Yes	Low
Marcusson *et al*[14]	RCT; split-mouth design	60 patients (21 male, 39 female) Median age 13.7 years, range 10.8 – 19.1 years	Number and severity of white spots assessed with modified Gorelick Index from after photographs	Randomisation – Yes Allocation concealment – Unclear Assessor blinding – Yes Dropouts described – Yes Sample justified – No Baseline comparison – Yes Inclusion/Exclusion criteria – Unclear Method error – Yes	Low
Twetman[13]	RCT; split-mouth design	20 patients; 22 pairs of premolars; extracted after 6 to 8 weeks. Mean age 15.5 years, range 13 – 17 years	White spots on extracted premolars after staining with erythrocin and evaluated under stereomicroscope (6–12x)	Randomisation – Unclear Allocation concealment – Unclear Assessor blinding – No Dropouts described – Yes Sample justified – No Baseline comparison – Unclear Inclusion/Exclusion criteria – No Method error – Yes	High

Table 1 *(continue)*

Reference	Design	Participants	Outcomes	Quality assessment	Risk of bias
Czochrowska *et al*[19]	RCT; split-mouth design.	7 patients, 9 pairs of teeth. Age range 11 – 13 years	Mineral loss and lesion depth on extracted premolars assessed with contact microradiography	Randomisation – No Allocation concealment – No Assessor blinding – No Dropouts described – Yes Sample justified – No Baseline comparison – No Inclusion/Exclusion criteria – Yes Method error – No	High
Gorton & Featherstone[16]	RCT; parallel groups	25 patients (4 drop outs; 8 male 13 female) Mean age 13.2 years, SD 1.9, range 11–18 years	Mineral loss and lesion depth on extrcated premolars assessed with microhardness	Randomisation – Yes Allocation concealment – Yes Assessor blinding – Yes Dropouts described – Yes Sample justified – No Baseline comparison – Unclear Inclusion/Exclusion criteria – No Method error – No	Low
Pascotto *et al*[17]	RCT; 2 parallel groups	14 patients (23 teeth) Age range 12–17 years	Mineral loss and lesion depth on extracted premolars using cross-sectional microhardness	Randomisation – Yes Allocation concealment – Unclear Assessor blinding – Yes Dropouts described – Yes Sample justified – No Baseline comparison – Yes Inclusion/Exclusion criteria – No Method error – No	Low
Compomer versus composite for bonding					
Chung *et al*[15]	RCT; split-mouth design	13 patients Mean age 13.4 years (including Chung)	Number and severity of white spots, assessed with modified Gorelick Index from before and after treatment photographs by one blinded examiner	Randomisation – Yes Allocation concealment – Yes Assessor blinding – Yes Dropouts described – Yes Sample justified – No Baseline comparison – Unclear Inclusion/Exclusion criteria – No Method error – Yes	Low
Millett *et al*[20]	CCT; alternate allocation; split mouth design	45 patients (13 male, 32 female) Median age 14.4 years, interquartile range 13.7 – 15.5 years	Number and severity of white spots assessed with modified Gorelick index from after treatment photographs	Randomisation – No Allocation concealment – No Assessor blinding – Yes Dropouts described – Unclear Sample justified – No Baseline comparison – Yes Inclusion/Exclusion criteria – No Method error – Yes	High

Table 1 *(continue)*

Reference	Design	Participants	Outcomes	Quality assessment	Risk of bias
Compomer versus GIC for banding					
Gillgrass *et al*[21]	RCT; split-mouth design	98 patients (32 males, 66 females;) Mean age males 19.1 years (SD3.7), females 17.8 years (SD3.0)	Number and severity of white spots assessed by clinical exam before and after treatment (Gorelick Index)	Randomisation – Yes Allocation concealment – Yes Assessor blinding – No Dropouts described – Yes Sample justified – No Baseline comparison – Unclear Inclusion/Exclusion criteria – No Method error – No	Moderate
Fluoridated versus non-fluoridated elastics					
Banks *et al*[22]	CCT; 2 parallel groups	49 expt (16 male, 33 female) Mean age 15.5 years, SD 3.5 45 control (15 male, 30 female) Mean age 16.5 years, SD 6.1	Number and severity of white spots - assessed with Enamel Decalcification Index	Randomisation – No Allocation concealment – No Assessor blinding – No Dropouts described – Yes Sample justified – Yes Baseline comparison – Yes Inclusion/Exclusion criteria – No Method error – No	High

fluoride varnish (Fluor Protector) alternately at each treatment visit. There were no significant differences between the control and experimental group in the proportion of patients with WSL (Peto OR 0.89; 95% CI 0.52–1.53). The study was judged to have a high risk of bias because following contact with the author it fulfilled one out of the four major methodological quality criteria (method of randomization) and in addition it failed to fulfill any of the minor methodological criteria.

Fluoridated versus non-fluoridated composite for bonding. One split-mouth CCT[12] compared a fluoridated composite (FluorEver; Macrochem Corp, Woburn, MA) with a non-fluoridated composite (Aurafill; Johnson & Johnson Dental Care Co, East Windsor, NJ). There was no significant difference in the number of WSL between the two materials (OR 0.00; 95% CI 0.00–1.52). However, there were only four cases of white spots in the 22 patients and these were all in the control group. This suggests that the sample size was too small. This study was assessed as a high risk of bias, because it fulfilled only one major methodological quality criteria (accounting for withdrawals and drop outs) and no minor criteria.

GIC versus composite for bonding. This comparison had the most included studies. Six studies compared GIC (experimental, fluoride group) and composite (control, non-fluoride group) for bonding brackets. The first trial[13] compared a conventional GIC (AquaCem; DeTrey, Dentsply, Konstanz, Germany) with a conventional composite resin (Concise; 3M Dental Products, St Paul, MN). They studied 22 premolars in 20 individuals. They used a split-mouth technique, with random allocation of the test material to either the right or the left. The study period was short as the teeth were extracted after 6–8 weeks. The assessment was carried out by visual inspection of the extracted teeth under stereomicroscope by two investigators, using a 4-point scale. There was no significant difference between the materials using this experimental technique, however, the number of teeth with white spots was high (15 out of 22). This is probably because of the method of assessment (you are more likely to see a white spot under a microscope). The odds ratio was estimated to be 0.00 (95% CI 0.00–5.33). The study was judged to be a high risk of bias. It fulfilled one major methodological quality criteria (reporting and analysis of withdrawals and drop outs) and one minor criteria (an estimation of measurement error was carried out).

The second trial[14] compared a conventional GIC (AquaCem; DeTrey, Dentsply, Konstanz, Germany) with a no-mix composite resin (Unite; Unitek, Monrovia, CA). They used a split mouth design on 60 patients with the two test materials being selected randomly for each jaw. White spots were assessed from pre- and post-treatment photographs by three judges using a four-point scale. Disagreements were resolved by consensus and an error analysis was carried out. The results show that the GIC quadrants had a significantly reduced number of white spots during orthodontic treatment (mean length of treatment 22 months) compared with the composite quadrants OR 0.35 (95% CI 0.13 to 0.86). The study was assessed as a low risk of bias. Although following contact with the author, the method of allocation concealment was not clear, there was no a priori sample size calculation or clear exclusion criteria, the study was well-designed and considered unlikely to have significant bias.

The third trial[15] compared a resin-modified GIC (Vitremer; 3M Dental Products, St Paul, MN) with a no-mix composite resin (Right-on; T.P. Orthodontics, La Porte, IN). This was a split mouth study with the upper right and lower left premolars bonded with the test material. The patients used a non-fluoride toothpaste so that the true effect of the fluoride in the material could be studied. White spot assessment was carried out from the before and after treatment photographs by one calibrated and blinded examiner using a 3-point scale. The test period was again short, as the premolar teeth were extracted after 4 weeks. There was no significant difference in the number of white spots between the two materials OR 0.00 (95% CI 0.00–1.52). The study was rated as having a moderate risk of bias, because it fulfilled two major criteria and only one minor criteria for methodological quality.

The fourth trial[16] compared a resin-modified GIC (Fuji Ortho LC; GC America Inc, Chicago, IL) with a light-cured composite resin (Transbond XT; 3M Unitek, Monrovia, CA). They compared two parallel groups with random allocation to either the test or experimental material. The sample size was small (21 individuals: 11 test and 10 control) and the study time was short, as premolars due for extraction as part of the treatment, were studied. This was a well-conducted study with proper randomization, allocation concealment and blinding and therefore the risk of bias was rated as low (Table 1). The outcome was the estimation of enamel mineral loss using microhardness testing. The results demonstrated significantly increased mineral loss with the light-cured composite, mean difference –645 vol%/μm (95% CI –915 to –375). This study investigated the secondary outcomes of the review and not the primary outcome. It was judged to be a low risk of bias, because it fulfilled all the major methodological criteria. However, it failed to fulfill any of the minor criteria.

The fifth study[17] also investigated the resin-modified GIC (Fuji Ortho LC; GC America Inc, Chicago, IL) and compared it with a conventional composite resin

(Concise; 3M Dental Products, St Paul, MN). The study was very similar to the previous study[16] involving two parallel groups with random allocation to the test and experimental material. There were also a small number of individuals (14 patients, 7 in each group) studied for a short time, as the teeth were extracted and the outcome was an estimation of enamel mineral loss using cross-sectional microhardness testing. Many results are presented representing different depths and distances from the bracket. Arends *et al.*[18] state that for microhardness measurements, the outer 25 μm should not be included; therefore, the data for mineral loss at a depth of 30 μm were chosen for comparison. There was no difference between the Knoop hardness values for the GIC (324.1 + 23.9) and the composite resin (322.4 + 26.1). The study has been assessed as a low risk of bias, because it fulfilled three major methodological criteria and one minor.

The sixth study[19] investigated a resin-modified GIC (Vitremer; 3M Dental Products, St Paul, MN) compared with a conventional composite resin (Concise; 3M Dental Products, St Paul, MN). The study used a split-mouth design with random allocation of 9 premolar pairs, in 7 individuals, to either the experimental or control material. The premolars were extracted after 4 weeks and the teeth subjected to contact microradiography to measure mineral loss and lesion depth of the surrounding enamel. There was a significant difference both between the mineral loss of enamel surrounding the experimental material (742.0 + 167.6 vol%/μm) and the control (1696.1 + 1211.1 vol%/μm) and the lesion depth of enamel surrounding the experimental material (18.0 + 6.0 μm) and the control (64.3 + 52.7 μm). The study was judged to have a high risk of bias, as it fulfilled one major and one minor methodological quality assessment. The author has been contacted and a reply is awaited.

Compomer versus composite for bonding. Two controlled clinical trials are included in this comparison. The first[15] was in the publication reported above, but in a different group of patients and compared a fluoride-containing compomer (Dyract Ortho; DeTrey, Dentsply, Konstanz, Germany) with a non-fluoride containing, no-mix composite resin (Right-on; T.P. La Porte, Indiana). The experimental time was short (4 weeks) and there was no statistically significant difference in the number of WSL between the two materials (OR 0.00; 95% CI 0.00–2.42). Again, the sample size was small. The study was judged to be a moderate risk of bias.

The second trial[20] investigated the same materials as the study above, but the study was longer with a mean treatment time of 21 months. A split-mouth design was used on 45 patients with compomer resin material, the alternately allocated treatment to either the right or left side of each arch. WSL were assessed from before and after clinical photographs, scored by a single experienced judge on a 4-point scale. There was no statistically significant (OR 0.22; 95% CI 0.02–1.07) difference between the materials. The study was considered to be a high risk of bias, as it fulfilled one major and one minor criterion for the methodological quality assessment.

Compomer versus GIC for banding. One trial[21] compared a fluoride-containing, light-cured compomer material (Band-Lok; Reliance Orthodontic Products, Itasca, IL) with a conventional non-fluoride containing, chemical cure GIC (Ketac-Cem; ESPE, Gmbh, Seefeld Oberbay, Germany) for banding molars in 98 individuals. This was a split-mouth study, with random allocation of materials to the left or right of the first arch and the opposite quadrant of the opposing arch. The mean time of banding was 20.3 months and in 8 individuals the white spot score was not obtained. Assessment of WSL was by visual inspection, before and after treatment, using a 4-point scale. There was no significant difference in the proportion of patients with new WSL between the two materials (OR 0.29; 95% CI 0.03–1.50). Following contact with one of the authors, the study was judged to be a moderate risk of bias, because it fulfilled three major (there was no assessor blinding), but no minor methodological criteria assessments.

Fluoridated versus non-fluoridated elastics. One controlled clinical trial with parallel groups,[22] alternately allocated to receive either fluoridated or non-fluoridated elastomeric ligatures (elastics to hold the wire in place) throughout treatment. The primary outcome was the number of patients with WSL at the end of treatment. This figure was high for both groups and there was no statistically significant difference in the odds ratio between the fluoridated elastics group (31 patients out of 49 with WSL) compared with the non-fluoridated elastics group (33 out of 45 with WSL), Peto OR 0.63 (95% CI 0.27–1.50). The study was judged to be a high risk of bias, because although it fulfilled all the minor criteria for methodological quality, it did not fulfill any of the major criteria. The main concerns of the reviewers about this study were the method of allocation (alternate) and the assessment blinding. One individual carried out the final recording and undertook an estimation of error; however, the assessor was one of three clinicians who had treated the patients and no method of blinding for allocation was discussed.

Discussion

This review has found some evidence that a daily sodium fluoride mouthrinse will reduce the severity of

demineralization associated with orthodontic appliances and that GIC used for bonding reduces the incidence and severity of WSL compared with a composite resin. However, considering the widespread use of fluoride products during orthodontic treatment, there is little evidence as to which method or combination of methods to deliver the fluoride is the most effective. Until high quality clinical trials are conducted, we would recommend that best practice is daily rinsing with 0.05% sodium fluoride mouthrinse. This is based on research carried out in non-orthodontic patients, which shows that regular supervised use of a fluoride mouthrinse[4], in addition to a fluoridated toothpaste,[23] is associated with a reduction in caries for children and adolescents; the principal age group of orthodontic patients.

It is clear that more research is required into the different modes of delivery. Most of the studies indicated that the fluoride product might have a beneficial effect, but the confidence intervals were wide and there were few statistically significant results. It is important to note that none of the studies fulfilled all the major and minor criteria for the assessment of methodological quality, and most of the studies failed to achieve even half. Only three studies included in this review[14,16] met all the explicit major criteria used to assess the validity of the study. In addition, only one study[22] had carried out an *a priori* sample size calculation. When future studies are planned, much more thought must be given to the design of the study to reduce bias and the number of patients required to show a significant difference, if one exists.

The way the fluoride is delivered is important. A fluoride mouthrinse will only work if it is used regularly by the patient and, therefore, relies on patient compliance to succeed. However, there is evidence to suggest that compliance with mouthrinsing is poor. One study[24] found that only 42% of patients rinsed with a sodium fluoride mouthrinse at least every other day. They also showed that those who complied least with fluoride rinsing regimens tended to have more WSL. A fluoride cement or elastic will release fluoride without help from the patient, and therefore might be more successful. In addition, these materials deliver the fluoride close to the bracket where it is most needed. However, many fluoridated materials release large amounts of fluoride initially, but the level drops rapidly and might not be sufficient to prevent decay over the whole course of orthodontic treatment.

When examining the effectiveness of a fluoride product in preventing dental decay, two aspects should be considered. First, whether the fluoride product reduces the number of WSL appearing during treatment and, secondly, whether it reduces the severity in terms of the size or area of the tooth surface affected or the amount of mineral lost or depth of the decay. Many studies used an index first described by Gorelick *et al.*[1] This is an ordinal scale of 0=no white spot to 3=frank cavitation. This index addresses the presence or absence of decay, and to a certain extent the severity, but not the area of tooth covered by the white spot, which may be of concern to the patient. Banks *et al.*[22] developed the Enamel Decalcification Index, which is also an ordinal index, but includes an assessment of the area covered. An assessment of size of the lesion is a useful outcome measure.

Several of the studies only recorded the appearance of the teeth at the end of the experiment. Ideally, the appearance of the tooth should be recorded before and after orthodontic treatment so that the change in appearance of the tooth is measured (incidence), not just the appearance at the end (prevalence). The measurement of both incidence and severity will depend upon the method of recording the WSL. There are two main methods of recording WSL: visual inspection and clinical photographs. Both methods have problems. The problem with visual inspection is that the examiner or examiners will require calibration at the start and regular recalibration throughout the experimental period, to ensure consistency of measurement. The length of the experiment might be quite long because, as discussed later, the product should ideally be tested over the entire length of orthodontic treatment. This can take between 18 and 30 months. A second problem with visual recording is blinding. To reduce bias the examiner should be blind to group allocation at the time of recording, which might complicate the way the experiment is run.

Photographs have the advantage of providing a permanent record of the appearance of the tooth. Assessment of the teeth can be carried out by several people independently or in groups, whereby a consensus can be achieved. The photographs can be placed in a random order and the judges blinded to group allocation. An error analysis can be carried out. In addition, because the assessment can be performed over a short period of time the problem of examiner drift, whereby an assessor might subtly change their assessment over time, will be reduced. The problem with photographs is achieving consistency in lighting, developing and reducing reflections that can mask or mimic WSL. However, with a careful photographic technique the advantages of photographs outweigh the potential disadvantages. There are a number of optical methods of measuring lesions on teeth.[25] These require specialized equipment, which would add considerably to the cost of a clinical study, but would provide an objective measurement of the amount of demineralization.

One variable that was not constant between the different studies was the length of time over which the

materials were studied. When a quantitative method of measuring the amount of mineral lost from enamel or the depth of a carious lesion is used, such as transverse microradiography or hardness testing, the tooth being examined has to be extracted and cut into sections.[9] Short experimental periods are inevitable, as delaying the extraction of the tooth will also delay the orthodontic treatment. However, a short experimental period might benefit materials that release a large amount of fluoride initially preventing WSL, but then the fluoride release drops off dramatically to a level that does not prevent decay. Ideally, the material should be tested over the entire length of orthodontic treatment.

When a product, such as a bonding material, can be applied to single teeth it is tempting to use an experimental design whereby the material being tested is used in two quadrants of the mouth and the control material is used in the other two quadrants. This is called a split-mouth design. The main advantage of the split-mouth design over a conventional parallel group design of study, in which the two materials are tested in two separate groups of individuals, is that the experimental material is tested in the same mouth, under the same conditions as the control material. In theory, any differences in outcome between the two materials is due only to their properties and not to other factors, such as differences in oral hygiene and diet between patients, that can occur in parallel studies or even differences of oral hygiene and diet over time within patients, that can occur in crossover studies. Because the number of confounding variables is decreased, the variability of the outcome measurement should be decreased. This will increase the power of the study and there is the potential that fewer patients will need to be recruited.

The split-mouth technique is very useful when examining outcomes in which the performance of one material will not affect the performance of the other, for example, a bond failure study. Unfortunately, when examining the ability of fluoride products to reduce decay, it is highly unlikely that the fluoride released will be confined to only the quadrants in which the experimental material has been placed and there will inevitably be some cross-over effect onto the control side. This will reduce the difference in outcome between the materials and reduce the power of the experiment to find a difference. We were not able to test the theory that split-mouth studies are less likely to produce a difference compared with parallel studies, because there were so few suitable studies. Until we understand how fluoride released on one side of the mouth will influence conditions on the other side, we suggest that the potential effects of a cross-over or contamination of the control area could lead to this study design being unsuitable and would recommend that a parallel design of study is used to examine the true effect of the fluoride material.

There were no studies examining the patient attitude to white spot lesions and their potential affect on the quality of life particularly 6 months or a year after treatment. This would be a useful further area of research.

A version of this review has been published in *The Cochrane Library*[26] (see www.CochraneLibrary.net for information). The results of a Cochrane Review can be interpreted differently, depending on people's perspectives and circumstances. Please consider the conclusions presented carefully. They are the opinions of the review authors and are not necessarily shared by the Cochrane Collaboration. Cochrane systematic reviews are regularly updated to include new research, and in response to comments and criticisms from readers. *The Cochrane Library* should be consulted for the most recent version of the review. If you wish to comment on this, or other Cochrane reviews of interventions for oral health, please send it to Emma Tavender, Cochrane Oral Health Group (emma.tavender@man.ac.uk).

Conclusions

1. Until high quality trials are conducted, we would recommend that best practice for orthodontic patients with fixed appliances is daily rinsing with a 0.05% sodium fluoride mouthrinse.
2. There is some evidence that use of a GIC, when bonding brackets, is more effective at preventing enamel demineralization and post-orthodontic WSL, than a conventional composite resin, but again the evidence is weak.
3. More, well-designed clinical trials are required.

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Contributors

Philip Benson was responsible for coordinating the review, collecting data, data interpretation, drafting and final approval of the article. Fiona Dyer, Declan Millett,

Nicola Parkin, Anwar Shah and Suzy Vine were responsible for data collection, critical revision and final approval of the article. Other contributors were Jayne Harrison (reviewing), Helen Worthington (statistics), Sylvia Bickley (searches) and Emma Tavender (copy editing). Philip Benson is the guarantor.

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