

Seal or Varnish? A randomised controlled trial to determine the relative cost and effectiveness of pit and fissure sealant and fluoride varnish in preventing dental decay

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**National Institute for
Health Research**

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Abstract

Seal or Varnish? A randomised controlled trial to determine the relative cost and effectiveness of pit and fissure sealant and fluoride varnish in preventing dental decay

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Background: Fissure sealant (FS) and fluoride varnish (FV) have been shown to be effective in preventing dental caries when tested against a no-treatment control. However, the relative clinical effectiveness and cost-effectiveness of these interventions is unknown.

Objective: To compare the clinical effectiveness and cost-effectiveness of FS and FV in preventing dental caries in first permanent molars (FPMs) in 6- and 7-year-olds and to determine their acceptability.

Design: A randomised controlled allocation-blinded clinical trial with two parallel arms.

Setting: A targeted population programme using mobile dental clinics (MDCs) in schools located in areas of high social and economic deprivation in South Wales.

Participants: In total, 1016 children were randomised, but one parent subsequently withdrew permission and so the analysis was based on 1015 children. The randomisation of participants was stratified by school and balanced for sex and primary dentition baseline caries levels using minimisation in a 1 : 1 ratio for treatments. A random component was added to the minimisation algorithm, such that it was not completely deterministic. Of the participants, 514 were randomised to receive FS and 502 were randomised to receive FV.

Interventions: Resin-based FS was applied to caries-free FPMs and maintained at 6-monthly intervals. FV was applied at baseline and at 6-month intervals over the course of 3 years.

Main outcome measures: The proportion of children developing caries into dentine (decayed, missing, filled teeth in permanent dentition, i.e. D₄₋₆MFT) on any one of up to four treated FPMs after 36 months. The assessors were blinded to treatment allocation; however, the presence or absence of FS at assessment would obviously indicate the probable treatment received. Economic measures established the costs and budget impact of FS and FV and the relative cost-effectiveness of these technologies. Qualitative interviews determined the acceptability of the interventions.

Results: At 36 months, 835 (82%) children remained in the trial: 417 in the FS arm and 418 in the FV arm. The proportion of children who developed caries into dentine on a least one FPM was lower in the FV arm (73; 17.5%) than in the FS arm (82, 19.6%) [odds ratio (OR) 0.84, 95% confidence interval (CI) 0.59 to 1.21; $p = 0.35$] but the difference was not statistically significant. The results were similar when the numbers of newly decayed teeth (OR 0.86, 95% CI 0.60 to 1.22) and tooth surfaces (OR 0.85, 95% CI 0.59 to 1.21) were examined. Trial fidelity was high: 95% of participants received five or six of the six scheduled treatments. Between 74% and 93% of sealants (upper and lower teeth) were intact at 36 months. The costs of the two technologies showed a small but statistically significant difference; the mean cost to the NHS (including intervention costs) per child was £500 for FS, compared with £432 for FV, a difference of £68.13 (95% CI £5.63 to £130.63; $p = 0.033$) in favour of FV. The budget impact analysis suggests that there is a cost saving of £68.13 (95% CI £5.63 to £130.63; $p = 0.033$) per child treated if using FV compared with the application of FS over this time period. An acceptability score completed by the children immediately after treatment and subsequent interviews demonstrated that both interventions were acceptable to the children. No adverse effects were reported.

Limitations: There are no important limitations to this study.

Conclusions: In a community oral health programme utilising MDCs and targeted at children with high caries risk, the twice-yearly application of FV resulted in caries prevention that is not significantly different from that obtained by applying and maintaining FSs after 36 months. FV proved less expensive.

Future work: The clinical effectiveness and cost-effectiveness of FS and FV following the cessation of active intervention merits investigation.

Trial registration: EudraCT number 2010-023476-23, Current Controlled Trials ISRCTN17029222 and UKCRN reference 9273.

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List of abbreviations

BNF	<i>British National Formulary</i>	ID	identification
CACE	complier average causal effect	MDC	mobile dental clinic
CDS	Community Dental Service	MHF	medical history form
CEAC	cost-effectiveness acceptability curve	MHRA	Medicines and Healthcare products Regulatory Agency
CHU-9D	Child Health Utility Index 9D	MIH	molar incisor hypomineralisation
CI	confidence interval	NICE	National Institute for Health and Care Excellence
CONSORT	Consolidated Standards of Reporting Trials	OR	odds ratio
CTIMP	clinical trial of an investigational medicinal product	p.p.m.	parts per million
CUA	cost-utility analysis	PEB	post-eruptive breakdown
DHQ	dental health questionnaire	PIS	participant information sheet
DMFS	decayed, missing, filled tooth surfaces in permanent dentition	PPI	patient and public involvement
DMFT	decayed, missing, filled teeth in permanent dentition	QALY	quality-adjusted life-year
DTF	Delighted-Terrible Faces scale	QATY	quality-adjusted tooth-year
FPM	first permanent molar	QoL	quality of life
FS	fissure sealant	REC	Research Ethics Committee
FSM	free school meal	SD	standard deviation
FV	fluoride varnish	SEWTU	South East Wales Trials Unit
HRQoL	health-related quality of life	SMM	structural mean model
ICC	intraclass correlation coefficient	SoV	Seal or Varnish?
ICDAS	International Caries Detection and Assessment System	TSC	Trial Steering Committee
ICER	incremental cost-effectiveness ratio	UHB	University Health Board
ICF	informed consent form	WIMD	Welsh Index of Multiple Deprivation
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use	WTP	willingness to pay

Plain English summary

Tooth decay is a very common problem. The biting surfaces of the first adult molar teeth, which erupt at the age of 6 years, are very vulnerable to decay. Rates of decay are especially high in children who live in disadvantaged communities. Two widely used treatments, fissure sealant (FS) (plastic coatings) and fluoride varnish (FV), can prevent decay. We do not know which works better or which is better value for money. This study aimed to answer this. Just over 1000 children were treated with either FS or FV over 3 years. After 3 years, 835 children were still taking part in the study, which was a sufficient number for the research teams to be able to see if one of the treatments was better than the other. Of the children who had the FV treatment, 17.5% had decay in their molars that was bad enough to need a filling or for the tooth to be taken out. In the sealant-treated group, 19.6% of children had decay in their first molars. Although fewer children treated with FV had tooth decay, this was not significantly different from the sealant-treated children. Over the 3 years, there was a cost saving of £68.13 per child in the FV group compared with those receiving sealants. Both treatments were acceptable to the children. The main conclusions from the study are that in a community programme such as this, there is no difference in the benefits gained from the treatments, although FV is slightly cheaper.

Scientific summary

Background

Dental caries (tooth decay) is among the most common diseases to affect humankind and correlates closely with social and economic deprivation. Within the mouth, teeth differ in their susceptibility to dental decay. This largely reflects the fact that dental plaque (oral biofilm) is more likely to form in specific areas. One such area is the occlusal (or biting) surface of first permanent molar (FPM) teeth. These teeth erupt at the age of 6 or 7 years and are particularly prone to decay shortly after they erupt. There are two preventative dental technologies that have the potential to be targeted specifically at the occlusal surfaces of FPMs: pit and fissure sealant (FS) and fluoride varnish (FV). These treatments have been used for several decades and have been shown to be effective in preventing dental caries when tested against no-treatment controls. However, it is not clear which treatment is the more clinically effective and cost-effective. An answer to this question would help NHS dental services to plan for more effective and efficient planning of preventative dental care.

Objectives

Primary objective

The primary objective of this study was to compare the clinical effectiveness of FS and FV in preventing dental caries in FPMs in children aged 6 and 7 years, as determined by the:

- proportion of children developing new caries on any one of up to four treated FPMs
- number of treated FPM teeth caries free at 36 months.

Secondary objectives

The secondary objectives of this study were to:

- establish the costs and budget impact of FS and FV delivered in a community/school setting and the relative cost-effectiveness of these technologies
- examine the impact of FS and FV on children and their parents/carers in terms of quality of life and treatment acceptability
- examine the implementation of treatment in a community setting with respect to the experience of children, parents, schools and clinicians.

Study design

A randomised controlled, assessor-blinded clinical trial with two parallel arms.

Setting

A Community Dental Service-targeted population programme delivered in mobile dental clinics (MDCs) in primary schools located in areas of high social and economic deprivation in South Wales.

Participants

Inclusion criteria

Children were eligible for inclusion if:

- they were aged 6 or 7 years and attended the schools participating in the current Cardiff and Vale University Health Board Designed to Smile programme
- the person with parental responsibility had provided written informed consent
- they had at least one fully erupted FPM free of caries into dentine.

Exclusion criteria

Children were ineligible for inclusion if:

- their medical history precluded inclusion [i.e. they had a history of hospitalisation for asthma, severe allergies or allergy to Elastoplast (Beiersdorf AG, Hamburg, Germany), which was determined from a medical history form (MHF) that was completed by parents]
- they had a known sensitivity to colophony, or any of the product ingredients (e.g. methylacrylate in FS, determined from a MHF that was completed by parents)
- they had any abnormality of the lips, face or soft tissues of the mouth that would cause discomfort in the provision of FS/FV
- they were currently participating in another clinical trial involving an investigational medicinal product (determined from a MHF that was completed by parents)
- they showed obvious signs of systemic illness (e.g. colds, influenza, chickenpox) (determined at baseline examination).

Methods

Treatments

Eligible participants was randomised to receive either FS or FV and remained on the intervention to which they were randomised for the duration of the study.

Resin-based FS was applied at baseline to included FPMs, including part-erupted upper teeth. Sealants were checked at 6-month intervals and deficiencies were repaired. FV was applied, using a standard clinical protocol, to all eligible FPMs at baseline and at 6, 12, 18, 24 and 30 months.

Clinical dental examination

Study participants were examined supine in the MDC, under a standard overhead dental clinical light, using a plane dental mirror and ball-ended probe at baseline and at 12, 24 and 36 months. Dental caries was recorded by trained and calibrated examiners, who were blinded to treatment allocation. Teeth were not dried prior to clinical dental examination. Gross debris was removed using a toothbrush.

Health economics

The costs associated with the interventions for each trial participant were collected and summarised into the following categories.

- Implementation costs of the interventions.
- Health-care utilisation costs associated with travel or caregiving/time off work for families.
- Costs associated with the schools (e.g. as a result of child absence). Published unit costs were used or, when these were unavailable, local financial records were used to value resources in monetary terms using 2015 as the price year.
- Utility data were captured using the Child Health Utility Index 9D, and quality-adjusted life-years (QALYs) and quality-adjusted tooth-years were calculated. A budget impact analysis was undertaken.

Treatment acceptability assessment and process evaluation

Treatment acceptability was assessed in three ways: (1) acceptability scales were completed by clinical staff, (2) acceptability scales were completed by children participating in the trial and (3) qualitative interviews were conducted with a subsample of children, their parents, school staff and clinical staff.

The acceptability of delivering this type of preventative intervention via a mobile dental unit in a school setting was also investigated through questionnaires and interviews with children, parents, school staff and clinical staff.

Statistical issues

All comparative analyses were carried out on an intention-to-treat basis (without imputation). The primary outcome (decayed, missing, filled teeth in permanent dentition, i.e. D_{4-6} MFT) was analysed using a logistic regression model to compare arms. The results for binary outcomes are presented as unadjusted and adjusted odds ratios (ORs) for the FV arm compared with the FS arm (the reference arm). All models were adjusted for the randomisation balancing variables, sex and baseline caries in the primary dentition.

Sample size

Based on existing local epidemiological data, for an individually randomised trial at a power of 80% with a significance level of 5%, at least 313 children per group were required for a comparison of caries incidence of 20% versus 30% at the 36-month follow-up.

Results

A total of 1016 children were randomised 1 : 1 to participate in the trial. Arms were well balanced for all key characteristics at baseline. At 36 months, 835 (82%) children underwent a final clinical examination, on which the following results are based. The number completing the FS arm was 418 and the number completing the FV arm was 417. The most common reason for not completing the trial was moving away from the area or moving to a school that was not participating in the trial, which was reported as lost to follow-up. The number of children who withdrew from the trial was five in the FS arm and seven in the FV arm.

Clinical outcome

Proportion of children developing caries into dentine

The proportion of children who developed dentine caries (D_{4-6} MFT) on at least one FPM at 36 months was broadly similar in both the FS (19.6%) and FV (17.5%) arms.

The OR of developing caries in the FV arm (compared within the FS arm) was 0.87 [95% confidence interval (CI) 0.61 to 1.23] in the unadjusted model, that is, children who received FV were slightly less likely to develop caries than those who received FS, but this difference was not statistically significant.

As sex and baseline caries prevalence were used to balance the randomisation, an adjusted model was also performed and was taken as the primary analysis. The OR for developing caries in the FV arm was 0.84 (95% CI 0.59 to 1.21) in the adjusted model.

To determine the impact of potential confounding factors, a covariate analysis of the primary outcome was undertaken from two perspectives: one at child level and one at school level.

Numbers for the child-level covariate analyses were substantially lower than for the primary outcome because of questionnaire non-response. The only covariates that were significantly associated with outcome were frequency of tooth brushing (OR 0.36, 95% CI 0.21 to 0.60) and toothpaste type (OR 0.45, 95% CI 0.27 to 0.75). Those brushing twice a day or more often were less likely to develop caries on their FPMs than those brushing once a day or less often. Those using children's or other toothpaste were less likely to develop caries on their FPMs at 36 months. None of the covariates altered the main effect for arm.

Proportion of first permanent molar teeth developing caries into dentine (D_{4-6} MFT)

In both the FS and FV arms of the trial, 7.5% of all teeth developed caries into dentine, required a restoration or were extracted. A multilevel model adjusted for the number of decayed primary teeth at baseline and sex confirmed that the difference between children receiving FS and those receiving FV was not statistically significant (OR 0.97, 95% CI 0.73 to 1.28; $p = 0.83$).

Number of first permanent molar tooth surfaces developing caries into dentine (D_{4-6} MFT)

Ordinal regression modelling was undertaken on the number of FPM surfaces developing caries in each child. Those children in whom between 5 and 20 surfaces were affected were combined into one group because of the small number of children in these categories. There was no statistically significant difference between those receiving FS and those receiving FV, the model having been adjusted to account for the number of surfaces with caries per child, the number of decayed primary teeth at baseline and sex (OR 0.85, 95% CI 0.59 to 1.21; $p = 0.363$).

Occlusal versus non-occlusal surfaces

Overall, the proportion of occlusal surfaces that had developed caries into dentine at 36 months was significantly greater than the proportion of smooth surfaces developing caries (6.4% vs. 1.1%). It is clear that the proportion of occlusal surfaces affected by dentine caries was remarkably similar in the FS and FV arms of the trial, at 6.5% and 6.3%, respectively. The difference between intervention arms in the proportion of smooth surfaces of FPMs developing caries observed at 36 months was also minimal (1.0% vs. 1.3%). No significant difference was observed between trial arms for the main effect or for the interaction of arm with surface type, indicating no differential effect of treatment on occlusal and non-occlusal surfaces (OR 1.25, 95% CI 0.89 to 1.77).

Fidelity

Trial fidelity was high: 95% of participants were treated at five or six of the six treatment visits. Overall, 71.6% of treatments were within the treatment window throughout the trial, and a further 26.1% were outside the schedule on only one occasion.

Health economics

The main findings of the health economic analysis were as follows.

- It is feasible to undertake a comprehensive health economic evaluation alongside a randomised controlled trial of preventative health technologies within the context of a MDC setting.
- The intervention costs of the two technologies were £74.12 for FS and £64.16 for FV per child over the course of the trial.
- The costs of the two technologies showed a small but statistically significant difference; the mean cost to the NHS (including intervention costs) per child was £500 for FS, compared with £432 for FV, a difference of £68.13 (95% CI £5.63 to £130.63; $p = 0.033$) in favour of FV.
- When a partial societal perspective was included (with intervention costs), the costs were £529 for FS and £457 for FV, with a mean difference of £71.96 (95% CI £7.21 to £136.71; $p = 0.029$) in favour of FV.
- The budget impact analysis at 3 years showed that FV resulted in a cost saving of £68.13 (95% CI £5.63 to £130.63; $p = 0.033$) compared with FS. In addition, when three different scenarios were examined, the results did not change and FV remained dominant.
- Owing to the non-significant numerical differences in outcomes, the incremental cost-effectiveness ratio (ICER) was very sensitive to very small numerical differences in outcomes. All outcomes showed a non-statistically significant difference or no clinically important differences between FS and FV and, thus, the ICER calculation should be treated with appropriate caution. However, results remained consistent across all three outcomes used in the health economic analysis, that is, FV was less costly than FS, with similar outcomes achieved.

- The cost-effectiveness acceptability curves (CEACs) showed that there was a 70% probability of FV cost-effectiveness at a societal willingness-to-pay (WTP) threshold of £20,000 per QALY.
- The model-based analysis to estimate the incremental cost per QALY over longer-term horizons showed consistent results with the results of the within-trial analysis, with fewer costs and small QALY gains achieved, which made FV dominant in the ICER calculation. The CEACs showed that there was a 99% and 96% probability of FV being cost-effective within a societal WTP threshold of £20,000 per QALY. However, there are a number of uncertainties in the model, particularly the dearth of evidence on longer-term costs and outcomes associated with FV and FS in a preventative dental health context.

Acceptability of fissure sealant and fluoride varnish treatments

An important element of the clinical trial was the determination of the acceptability of FS and FV treatments. An acceptability score (called the Delighted–Terrible Faces scale), which was completed by the children immediately post treatment and in subsequent interviews with children and parents, demonstrated that both interventions are acceptable to children.

At baseline, the children in the FV arm were significantly more likely than those in the FS arm to report being happy (OR 0.38, CI 0.29 to 0.50; $p < 0.001$), with this situation being reversed at the final treatment at 30 months (OR 3.63, 95% CI 2.60 to 5.05; $p < 0.001$). In the course of the trial, those receiving FS became happier as the trial progressed; in contrast, in the FV arm there was a modest decrease in the number of children who chose a happy face.

Perceptions of undergoing treatment were influenced by aspects of treatment (especially taste) but also wider factors associated with a child-friendly MDC. Ultimately, the high number of children completing the trial can be taken as evidence of the acceptability of these interventions delivered in this setting. Acceptability to parents and school staff was also high.

Adverse effects

No adverse effects were reported as a result of the treatments provided.

Conclusions

The findings of this trial demonstrate that, in community oral health programmes targeted at children who are at high risk of caries, the application of FV as a caries-preventative measure will result in caries prevention that is not significantly different from that achieved by applying and maintaining FS for 36 months. There is a cost saving of £68.13 per child treated, using FV compared with the application of FS over this time period. Both treatments are acceptable to children aged 6–10 years, and acceptability to parents and to schools was also high.

Trial registration

This trial is registered as EudraCT number 2010-023476-23, ISRCTN17029222 and UKCRN reference 9273.

Funding

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Chapter 1 Introduction, background and objectives

Introduction

Dental caries (tooth decay) is among the most common diseases to affect humankind. In 2010, it was estimated that 35% of the global population, that is, 2.4 billion people, had untreated caries in their permanent dentition.¹ The NHS in England spends around £3.4B per year on dental services, and it is estimated that the private market accounts for a further £2.3B annually.²

Dental caries results from the metabolism of sugars by bacteria that are normally resident in the oral cavity. The acids produced cause the demineralisation (breakdown) of the tooth surface. Initially, the caries lesion is confined to the dental enamel. In its early stages, the disease process can be halted or even reversed by a process known as remineralisation. This is facilitated by the presence of fluoride at the interface between the tooth surface and the overlying biofilm of the dental plaque.

Untreated, the disease process continues to involve the underlying dentine and eventually the dental pulp becomes inflamed, resulting in pain: toothache. Once the dentine is involved, the tooth requires a restoration to halt caries progression. Ultimately, an inflamed pulp will die and a dental abscess may result. Resolution will require either root-filling or the extraction of the tooth.

The past four decades have seen great improvement in oral health in England and Wales. In 1973, the mean number of decayed, missing, filled teeth in permanent dentition (DMFT) in 15-year-olds was 8.4.³ By 2013 this had fallen to 1.4.⁴ This improvement is widely attributed to the introduction and the widespread use of fluoride-containing toothpaste in the 1970s. However, improvements in oral health have not been uniformly distributed across the population.

Children at risk of dental caries

Mean population values of dental caries prevalence mask an important fact. Similar to many chronic, lifestyle-associated diseases, caries prevalence is markedly linked to social and economic deprivation,^{5,6} and the prevalence is markedly skewed. At the age of 5 years, the prevalence of dental decay in children resident in the most deprived localities is more than twice that of children living in the least deprived communities. As oral health has improved, dental caries has become concentrated in children from poorer backgrounds.

Teeth at risk of dental caries

Individual teeth differ in their susceptibility to dental decay. This largely reflects the fact that dental plaque (oral biofilm) is more likely to form in specific areas. One such area is the occlusal (or biting) surface of molar teeth. This fissured surface predisposes teeth to oral bacteria multiplying in the depths of the fissures and forming an environment favourable to the fermentation of sugars into acid.

The first permanent molars (FPMs) erupt at the back of the mouth around 6 years of age. The occlusal surface of these teeth is particularly prone to dental caries, often within a short period of eruption into the mouth. Management of occlusal caries on permanent molars has proven to be a great challenge to the dental profession.⁷ Occlusal caries accounts for the majority of affected tooth surfaces in adolescents and adults.⁸⁻¹¹

It is, therefore, apparent that preventing dental caries on the occlusal surfaces of FPMs is a key objective in preventative dental care. These surfaces represent the surfaces most susceptible to decay and are present in susceptible children. Actions to prevent and arrest dental caries, targeted at these surfaces, have the potential to significantly improve oral health and to address inequalities.

Preventative dental technologies

There are two preventative dental technologies that have the potential to be targeted specifically at occlusal surfaces of FPMs: pit and fissure sealant and fluoride varnish (FV). The terms 'pit and fissure sealant' and 'fissure sealant' (FS) refer to the same material. Unless referring to the term used specifically by a referenced source, the term FS is used throughout this report.

Pit and fissure sealant

Pit and fissure sealant contains a bisphenol A and glycidyl methacrylate (bis-GMA) resin, which hardens on exposure to light. It is applied to the tooth surface using acid-etch technology. FS prevents dental caries by physically obliterating the pit and fissure system that has great potential to harbour cariogenic organisms. Eliminating the pit and fissure system removes this ecological niche and reduces the initiation of caries in this highly susceptible site. First developed in the 1960s, FS is an established technology and is widely used in clinical practice.

Numerous studies have investigated the clinical effectiveness of FS. A 2013 Cochrane systematic review¹² of sealants for preventing dental decay in the permanent teeth concluded that, in 12 trials in which resin-based sealants were compared with no sealant controls, the sealed teeth were significantly less likely to be carious at 2 years' follow-up [odds ratio (OR) 0.12, 95% confidence interval (CI) 0.07 to 0.19], although five of these trials were conducted in the 1970s, when caries prevalence was higher than it is now. The authors of the review concluded that the application of sealants was recommended to prevent and control dental caries. They found that the application of FS to occlusal surfaces of permanent molars was clinically effective when compared with unsealed control teeth up to 48 months but, beyond that time, effectiveness was uncertain. They further concluded that, although sealing was effective in high-risk children, evidence in other circumstances is scarce, and they were unable to achieve a primary objective of determining the effectiveness of sealants in relation to the baseline prevalence of dental caries in the population.¹²

Fluoride varnish

The caries-preventative effect of fluoride has been recognised for > 100 years. Evidence arising from ecological studies in the early twentieth century linked the presence of fluoride in the public water supply to reduced caries prevalence in the population.¹³ Subsequently, fluoride has been incorporated into a range of caries-preventative products for both professional use and self-use.

Fluoride primarily exerts cariostatic properties by a topical effect.¹⁴ The presence of fluoride at the tooth surface prevents demineralisation of the dental enamel and encourages remineralisation.

Fluoride-containing varnishes were developed in the 1960s. They contained fluoride at a much higher concentration [22,600 parts per million (p.p.m.)] than that present in water fluoridation programmes (0.5–1 p.p.m. fluoride) or toothpaste (1000–1500 p.p.m. fluoride). FVs were developed to prolong the contact of fluoride ions with the tooth surface, thereby enhancing their cariostatic effect.

The most widely used FV preparation in the UK is Duraphat® varnish [Colgate-Palmolive (UK) Ltd, Manchester, UK], marketed by Colgate®. This product contains 5% of sodium fluoride (22,600 p.p.m. of fluoride). Owing to the high fluoride content, the product is licensed as a prescription-only medicine and can be prescribed only by a medical or dental professional. FV is designed for application by a dental professional to specific at-risk tooth surfaces or early caries lesions. The recommended frequency of application is 2–4 times per year.

The clinical effectiveness of FV has been the subject of a recent Cochrane systematic review.¹⁵ The authors identified 13 studies that compared FV with a placebo or no treatment, and concluded that the pooled decayed, missing, filled tooth surfaces in permanent dentition (DMFS)-prevented fraction was 43% (95% CI 30% to 57%; $p > 0.0001$). However, the reviewers reported that the quality of the evidence was moderate, as it mainly included studies that were at a high risk of bias with considerable heterogeneity.¹⁵

Fissure sealant versus fluoride varnish

From the above reviews it is evident that both FS and FV are effective caries preventative agents. The question arises, therefore, as to which is the more effective, particularly in relation to the prevention of dental caries in FPMs.

Ahovuo-Saloranta *et al.*¹⁶ have recently published a Cochrane systematic review on the relative effectiveness of FS versus FV. This updates a previous version of the review published in 2010.¹⁷ The review identified four trials that had compared resin-based FS with FV. Two of these four studies, involving 358 children, suggested that, compared with FV, FS prevented more caries in FPMs at 2-year follow-up. The pooled OR was 0.65 (95% CI 0.50 to 0.94; $p = 0.02$). The authors stated that the body of evidence was assessed as low. Ahovuo-Saloranta *et al.*¹⁶ concluded that the conclusion of the updated review remained the same as the last update in 2010, that is, as a result of the limited number of data available it was not possible to draw clear conclusions about possible differences in effectiveness for preventing or controlling dental caries on occlusal surfaces of permanent molars.

The importance of establishing the relative clinical effectiveness, cost-effectiveness and patient preferences in relation to fissure sealant or fluoride varnish

Although the relative clinical effectiveness of FS and FV is important, a number of other factors should also be considered when choosing between these technologies.

Application and equipment

The application of FS requires the use of the acid-etch technique to achieve adhesion of the sealant to the tooth surface. Adequate moisture control is known to be a critical component of achieving a satisfactory bond.¹⁸ This means that sealants can reasonably be applied only in the confines of a 'dental surgery', be that fixed or mobile. The use of a '3-in-1' water/air spray is required, along with adequate aspirating facilities.

In contrast, the application of FV is much less technique sensitive and does not require the degree of specialist equipment needed for sealant placement. FV can simply be painted onto teeth using a small brush. Moisture control using cotton wool rolls or pads is sufficient. As a result, FV can be applied in a school medical room or other private location and does not necessarily need to be done within a clinic or traditional health-care setting.

Personnel required for placement

Whereas FS can be applied only by a dentist, dental therapist or dental hygienist in the UK, FV can be applied by an appropriately trained dental nurse. These factors raise the question of the relative costs associated with providing either FS or FV. Although the equipment and personnel costs required to provide FS are potentially higher, these need to be offset against the requirement for FV to be applied every 6 months and the single application and subsequent periodic check-up/top-up required for FS.

Patient acceptability

A further consideration is the relative acceptability of FS and FV to patients. At the age of 6 years, children may have limited experience of dental care. The more technically involved procedure of FS application may pose a greater challenge to an anxious or nervous child than the apparently more straightforward application of FV.

Approaches to improve oral health

There are three main approaches to improving oral health: a whole-population approach, a targeted-population approach and a high-risk individual approach.¹⁹

The Designed to Smile programme in Wales, part of the Welsh Government's National Oral Health Improvement Programme, takes a targeted population approach. There are several elements to the Designed to Smile programme, one of which is a FS scheme. This work is delivered in schools via the Community Dental Service (CDS) using mobile dental clinics (MDCs). This setting provided the backdrop to the current study.

To ascertain whether FS or FV is the more effective technology in preventing occlusal caries in FPMs is of importance to the NHS. This was recognised in the call by the National Institute for Health Research Health Technology Assessment Board, which commissioned the research reported here. In addition to clinical effectiveness, cost-effectiveness is of interest. As discussed above, FV requires less time than FS and can be applied by staff with less training. However, although FV requires twice-yearly application, FS require only periodic checking and maintenance. It is therefore possible that the technologies will differ in their costs and, thus, in their cost-effectiveness.

Finally, the preference of children and their parents for FS or FV merits investigation. The less invasive nature of FV placement compared with FS placement means that examination of the relative acceptability of these treatments is required.

The aims and objectives of the trial were, therefore, as follows.²⁰

Trial aims and objectives

Trial aim

The overall aim of the study was to identify and compare the relative clinical effectiveness and cost-effectiveness of two established technologies, FS and FV, for the prevention of dental caries in FPM teeth in children aged 6 or 7 years.

Trial objectives

Primary objective

The primary objective of this trial was to compare the clinical effectiveness of FS and FV in preventing dental caries in FPMs in 6- and 7-year-olds, as determined by the:

- proportion of children developing new caries on any one of up to four treated FPMs
- number of treated FPM teeth that are caries free at 36 months.

Secondary objectives

The secondary objectives of this trial were to:

- establish the costs and budget impact of FS and FV delivered in a community/school setting and the relative cost-effectiveness of these technologies
- examine the impact of FS and FV on children and their parents/carers in terms of quality of life (QoL) and treatment acceptability measures
- examine the implementation of treatment in a community setting with respect to the experience of children, parents, schools and clinicians.

Chapter 2 Methods

Trial design

The study was a Phase IV randomised, allocation-blinded, two-arm, parallel-group trial. The participants were randomised on a 1 : 1 allocation ratio to receive one of:

- resin-based FS
- FV.

There were no significant changes to the trial methodology after trial commencement. With the exception of some minor changes to improve the return rate of follow-up questionnaires, the trial was conducted as per the original protocol.²⁰

Approvals obtained

The Research Ethics Committee (REC) for Wales 3 (formerly known as the REC for Wales) approved the study on 15 February 2011 (reference 11/MRE09/6). The details of the REC and the NHS Research and Development department approvals and clinical trials authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA) are provided in *Appendices 1–3*.

Participants

The target population were children aged 6 or 7 years attending primary schools in designated Communities First areas; the Welsh Government has identified these localities as areas of social and economic deprivation. All children in such schools are deemed to be at high risk of caries, according to Public Health England and the Scottish Intercollegiate Guidelines Network, and qualify for FS/FV application.^{21,22}

Participant selection and eligibility criteria

Children were considered eligible to join the trial if they met all of the inclusion criteria and none of the exclusion criteria.²⁰ It was possible to assess whether or not children met some of these criteria prior to a clinical dental examination; however, for other eligibility criteria, examination by a dentist was required.

Inclusion criteria

Children were eligible for inclusion if:

- they were aged 6 or 7 years and attended the schools participating in the current Cardiff and Vale University Health Board Designed to Smile programme
- the person with parental responsibility has provided written informed consent
- they had at least one fully erupted FPM free of caries into dentine.

Exclusion criteria

Children were ineligible for inclusion if:

- their medical history precluded inclusion [i.e. those with a history of hospitalisation for asthma, severe allergies or allergy to Elastoplast (Beiersdorf AG, Hamburg, Germany), which was determined from a medical history form (MHF) that was completed by parents]

- they had a known sensitivity to colophony, or any of the product ingredients (e.g. methylacrylate in FS, determined from a MHF that was completed by parents)
- they had any abnormality of the lips, face or soft tissues of the mouth that would cause discomfort in the provision of FS/FV
- they were currently participating in another clinical trial involving an investigational medicinal product (determined from a MHF that was completed by parents)
- they showed obvious signs of systemic illness (e.g. colds, influenza, chickenpox; determined at baseline examination).

Recruitment into the trial

Number of participants

It was planned to recruit 920 participants, who would be randomised equally ($n = 460$ per arm) to the two technologies (FS and FV) investigated in this trial. The statistical justification for this number is discussed below.

Recruitment of schools

Eligible schools involved in the Cardiff and Vale University Health Board (UHB) CDS Designed to Smile programme were invited to participate in the trial. The trial management team visited those schools that expressed an interest in participating to discuss the practical and logistical aspects of the trial. When applicable, agreement to participate in the trial was documented.

Recruitment of participants

In line with the procedures for informing parents of children of the existing Designed to Smile programme, teachers distributed invitation packs to children for them to take home to their parents.

The following documents were included in the invitation packs:

- participant information sheet (PIS) for parents (see *Appendix 4*)
- MHF (see *Appendix 5*)
- informed consent form (ICF) (see *Appendix 6*).

Participant information sheet for parents

The PIS was developed in conjunction with a parents' group and approved by the REC (detailed in *Design of study materials and strategy for maximising questionnaire follow-up rates*). The PIS contained all of the necessary information for a parent or legal guardian to make an informed choice about their child's participation in the trial, as detailed in section 4.8 of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) *Guideline for Good Clinical Practice*.²³

Medical history

The medical history of potential participating children was ascertained by asking their parents or legal guardian to complete a MHF. Data were collected that specifically related to allergies, asthma (including whether or not this had resulted in hospitalisation) and sensitivity to constituents of either FS or FV, and if the child was currently participating in a clinical trial involving an investigational medicinal product. Whether or not the child was registered with a general dental practitioner was also ascertained.

Following a child's enrolment into the trial, any changes to their relevant medical history (as described above) was established via a brief MHF (see *Appendix 7*), which was sent to parents in advance of the annual clinical dental examination at 12 and 24 months. Parents were instructed to complete and return the MHF to the dental team only if there had been a change in their child's relevant medical history.

Informed consent

So that the trial could be conducted as pragmatically as possible, the consent process from the existing CDS FS programme was utilised, in that consent was provided remotely by parents completing consent forms at home and returning them to the school via their children. The consent rates for the existing FS programme are usually > 70% (depending on the school); therefore, effectively communicating the concept of the trial to parents without negatively affecting recruitment was key to the success of the trial. Given the setting and the low-risk nature of the trial, obtaining consent remotely was successfully justified to the REC.

The PIS included in the Seal or Varnish? (SoV) invitation pack introduced the trial to the parents and asked them to take the time to read the PIS before deciding whether or not they wanted their child to participate. Parents were also informed of the option for their child to enter the existing Designed to Smile programme instead of the trial. Explicit in the PIS was the opportunity to discuss any aspect of the trial with a member of the trial team over the telephone. A dedicated telephone number was provided for this purpose, with the provision for parents to leave a telephone number and e-mail address to be contacted by a member of the trial team at the next available opportunity. Parents were also asked to discuss the trial with their child.

After considering the information provided in the SoV invitation pack, and discussing the trial with a member of the trial team (if required), parents who wanted their child to participate were asked to sign and date the ICF (see *Appendix 6*). They were also asked to confirm on the ICF that they had been given the opportunity to discuss the trial with a member of the trial team or, alternatively, if they did not require any further information, to make a decision regarding their child's participation.

Children returned the completed ICF and MHF forms to their class teacher. On receipt of the ICF and MHF, a designated member of the SoV MDC team liaised with an appropriate member of school staff to verify that the name and signature on the ICF were in agreement with the school's records for the person with parental responsibility for that child.

Interventions

Study setting

The study interventions took place in the MDC, which visited schools in areas of high social and economic deprivation in the Cardiff and Cwm Taf Health Board areas in South Wales, UK. The MDCs were operated by the CDS, Cardiff and Vale UHB, under the Designed to Smile programme,²⁴ which was a national oral health improvement programme.

Technologies evaluated

The two technologies evaluated in this trial (FS and FV) are well established and have been used routinely for several decades to prevent dental caries, as discussed in *Chapter 1*. Eligible participants were randomised to receive either FS or FV and remained on the intervention to which they were randomised for the duration of the study.

Pit and fissure sealant

The FS used was Delton® Light Curing Opaque Pit and Fissure Sealant (Dentsply Ltd, Stonehouse, UK; CE0086). This is one of the most commonly used FS brands in the UK. FS was supplied as 2.7-ml bottles for multiple applications and applied topically as a thin layer to the occlusal surface of eligible FPMs. The standard clinical protocol, as described by the product manufacturers, was used to apply the FS (*Box 1*). The full details of the clinical protocol for FS application are given in *Appendix 8*.

The initial application of FS took place within 2 weeks of the baseline dental examination and was performed by a suitably qualified and trained dental hygienist. In the case of partially erupted molars, sealant was applied if sufficient tooth surface was available. This situation was most common in the case of upper molars. The same two dental hygienists provided treatments throughout the trial using two MDCs.

BOX 1 Procedure for application of FS

1. Prior to sealing, if necessary, teeth are cleaned with a toothbrush.
2. The tooth is isolated using dry guards/cotton wool rolls and saliva ejectors to aid moisture control.
3. The tooth surface is dried.
4. The etchant is applied to all the pits and fissures and a few millimetres beyond the final margin of the sealant for 30–60 seconds in accordance with the manufacturer's instructions.
5. The etchant material is washed from the tooth for at least 30 seconds and the tooth dried until it has a chalky, frosted appearance. Teeth that fail to etch properly are re-etched for a further 20 seconds. Great care is taken to avoid salivary contamination, as there is agreement that moisture contamination at this stage of the process is the most common cause of sealant failure.
6. The sealant material is applied to the occlusal surface and cured by shining a polymerisation light on the tooth surface for at least 20 seconds.
7. The sealant is evaluated visually and tactically and an attempt is made to dislodge it with a probe. Any deficiencies in the material are repaired to ensure an intact sealant surface.

The condition of the FS was re-examined at 6, 12, 18, 24 and 30 months. FS was reapplied if the existing sealant had become detached or if occlusal coverage was considered insufficient as a result of either further eruption of the tooth or part of the sealant becoming lost.

All applications of FS were documented on treatment record forms, which captured the date, batch number, participant identification (ID) number and number of teeth (one to four) treated.

Fluoride varnish

The FV used for evaluation in the study was Duraphat 50 mg/ml dental suspension (PL 00049/0042), equivalent to 22,600 p.p.m. fluoride. This is the most commonly used FV brand in the UK. FV was supplied in 10-ml tubes for multiple applications and applied topically as a thin layer to the pits, fissures and smooth surfaces of eligible FPMs. As per the Duraphat summary of product characteristics (see *Appendix 9*), the dosage per single application did not exceed 0.4 ml. The standard clinical protocol was used to apply the FV, as described in *Box 2*.

The initial application of FV occurred within 2 weeks of the baseline dental examination and was performed by a qualified and trained dental hygienist in accordance with the conventional clinical protocol established by the CDS (see *Box 2*). FV was reapplied at 6, 12, 18, 24 and 30 months, that is, on six occasions at 6-monthly intervals in the course of the trial. The full details of the clinical protocol for FV application are given in *Appendix 10*.

BOX 2 Procedure for application of FV

1. Prior to FV application, teeth are cleaned with a toothbrush if necessary.
2. The tooth is isolated using a cotton roll in the buccal sulcus.
3. The tooth is dried using a cotton roll.
4. A thin layer of FV is applied to the pits, fissures and smooth surfaces of FPMs using a disposable microbrush.
5. The cotton roll is removed from the buccal sulcus.
6. This procedure is repeated for all FPMs included in the trial.
7. The child is advised not to eat or drink for 30 minutes and not to brush their teeth for 4 hours after application.

All applications of FV were documented on treatment record forms, which captured the date, batch number, participant ID number and number of teeth (one to four) treated.

Clinical assessments

Participant eligibility

The demographic and medical history information collected from the parents was reviewed to determine if the child met the inclusion/exclusion criteria prior to a clinical examination. Children considered eligible underwent a baseline clinical examination to determine their eligibility, based on the clinical inclusion/exclusion criteria detailed in *Inclusion criteria* and *Exclusion criteria*.

Clinical dental examination

Study participants were examined in the MDC while supine under a standard overhead dental clinical light, using a plane dental mirror and a ball-ended probe. The probe was used only to remove debris and to determine surface texture. It was not used to probe for cavitation. Teeth were not dried prior to clinical dental examination. Gross debris was removed using a toothbrush.

Caries assessment using International Caries Detection and Assessment System

Caries status was assessed and recorded at baseline, for all children considered eligible, by trained and calibrated dentists using conventional diagnostic caries criteria at the d1/D1–d6/D6 level in accordance with nationally recognised diagnostic criteria.²⁵ Data were recorded using charts specifically designed for the collection of International Caries Detection and Assessment System (ICDAS) dental codes²⁶ (see *Appendix 11*). An assessment of molar incisor hypomineralisation (MIH) was also carried out.

Further clinical examination, including ICDAS caries assessment, was performed at 12-month intervals for 36 months. Experienced community dental officers undertook the clinical dental examinations. A total of six officers were used during the study, with one examiner involved in all years of the project.

Training and calibration

An intensive training and calibration exercise was undertaken in advance of each round of annual clinical examinations. Prior to each calibration exercise, the examiners were asked to complete the online e-learning package developed by the ICDAS team.²⁶ At each calibration event, the examiner team received an interactive lecture to review the ICDAS caries criteria. The calibration exercise was based on projected images of 74 extracted primary teeth. The gold standard was determined by Professor Chris Deery (a trained and calibrated ICDAS examiner), who provided the images. At each calibration exercise, the images were projected under standardised conditions and compared with the gold standard examiner. The caries code (the second digit of the ICDAS code) was recoded as 0, 'free of caries into dentine' (caries code 0–3), and 4, 'caries at ICDAS level 4 or higher', that is, 'caries into dentine' (caries code 4–6). Calibration was based on these categorisations at the 'caries into dentine' level.

As part of the annual caries assessment, approximately 5% of study participants were re-examined to determine intra-examiner reproducibility. The details of the analysis of ICDAS caries data are provided in *Statistical methods*.

Nomenclature for recording dental caries in the Seal or Varnish? trial

In the SoV trial dental caries was recorded using ICDAS.²⁶ As there is potential for confusion between the different codes and thresholds used to describe dental caries when using ICDAS and previous caries indices/scoring systems, *Table 1* describes the terms used to define thresholds and levels of dental caries experience.

In this study, dental caries status is described using the following principal terms: caries free, free of caries into dentine, enamel caries and dentine caries.

TABLE 1 The terms used to describe dental caries status in the SoV clinical trial

Terms used in this study (designation)	ICDAS caries codes	Traditional caries scores, (e.g. BASCD, WHO)	Notes
Caries free	00	Sound	Describes the condition as free of either enamel or dentine caries
Free of caries into dentine	00, 01, 02 and 03	Sound, D1 and D2	This is the status traditionally regarded as 'caries-free'. This is the principal diagnostic level used for both primary and secondary outcomes in the study
Enamel caries (d ₁₋₃ /D ₁₋₃)	01, 02 and 03	D1 and D2	Caries lesions limited to enamel
Dentine caries (d ₄₋₆ /D ₄₋₆)	04, 05 and 06	D3, both cavitated and non-cavitated	Caries lesions involving dentine, also referred to as obvious dental decay

BASCD, British Association for the Study of Community Dentistry; WHO, World Health Organization.

Treatment acceptability assessment

Treatment acceptability was assessed in three ways. A modified version of the Delighted–Terrible Faces (DTF) scale^{27,28} was used with children to determine participant acceptability (see *Appendix 12*). During the clinical placement of the technologies under investigation, the treating dental hygienist and dental nurse recorded the following indicators of participant acceptability and adverse outcomes: vomiting, crying, gagging, excessive arm/leg movements and other signs of distress.²⁹ As part of the process evaluation, children and their parents from each trial arm were interviewed in order to compare their experiences of FS and FV treatment (see *Chapter 5*).

Caries risk-related habits

For children deemed eligible to participate in the trial, information relating to the caries risk-related habits was obtained via a dental health questionnaire (DHQ) (see *Appendix 13*) sent to parents at baseline and at 12, 24 and 36 months post treatment.

The questionnaire asked about tooth brushing frequency, if the child brushed on their own or with parental assistance, the type of toothpaste used and the quantity of toothpaste dispensed to the toothbrush. An enquiry was also made as to the age at which tooth brushing started. The use of mouthwash, fluoride drops and fluoride tablets was determined, as was any previous application of FV by the child's own dentist. Attendance at a dentist outside the Designed to Smile programme was ascertained, as was the frequency of dental attendance. Parents were asked about lifetime residency in South Wales. The annual questionnaire also collected data on dietary habits, with an emphasis on the frequency of the consumption of sugar-rich food and drinks. The remaining questions enquired about the use of dental services, which informed the economic analysis of the trial.

Dental care during the trial

Parents were asked for details of their child's dentist. The principal investigator wrote to the dentist and informed them that the child was participating in the SoV trial. Dentists were asked to refrain from providing FS or FV treatment for the duration of the study. For children who were patients of the CDS, a flag was placed on their dental record to indicate that they were participants in the SoV study and therefore should not receive FS or FV treatments.

Children and their parents continued with their usual oral hygiene regime, details of which were gathered via the annual questionnaire detailed in *Caries risk-related habits*.

Participant flow

Participant flow through the trial is illustrated in *Figure 1*.²⁰

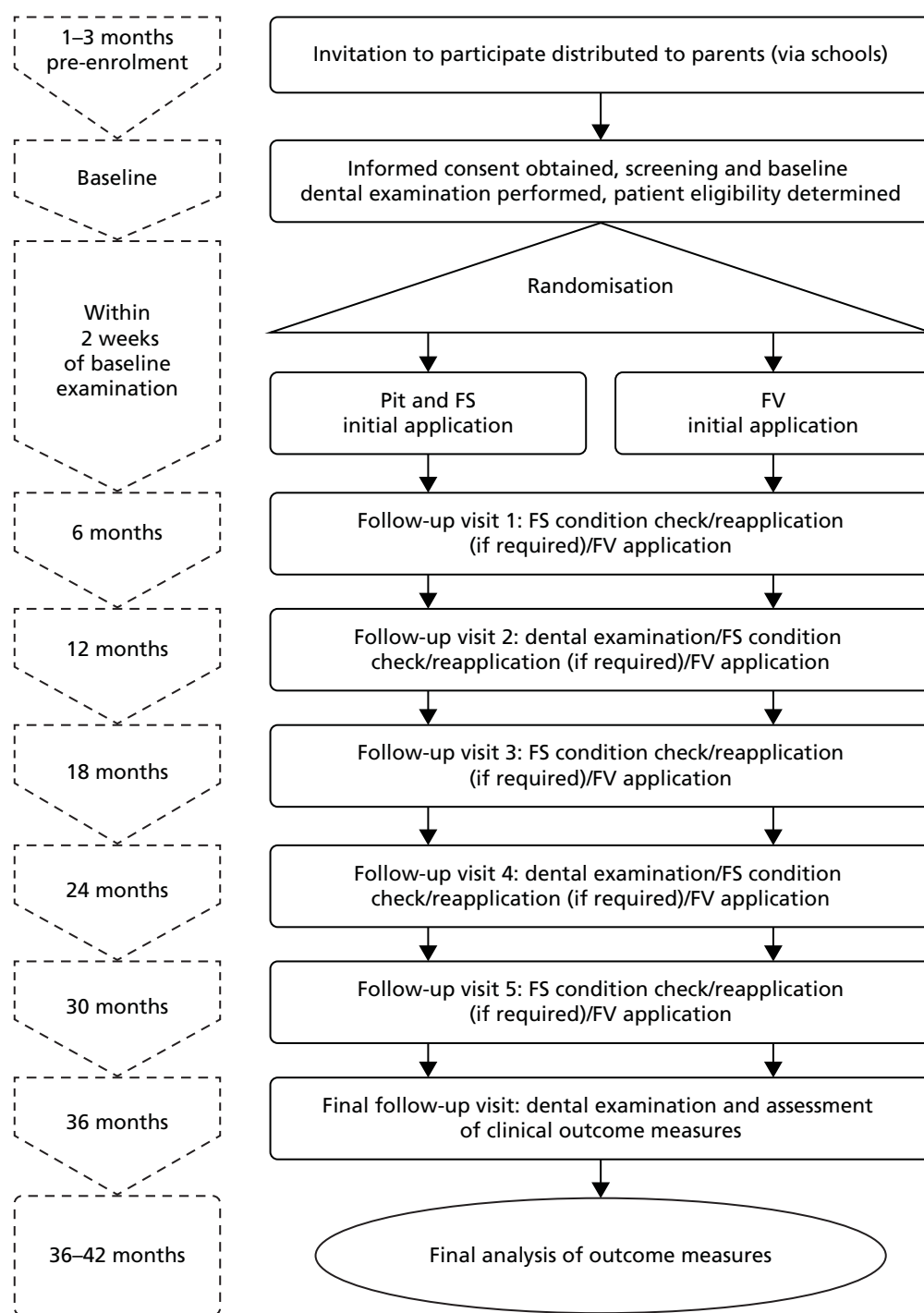


FIGURE 1 Participant flow diagram.²⁰

Data collection regime

The data collection regime is shown in *Table 2*.

TABLE 2 Data collection regime

Data type	Prior to baseline evaluation	Baseline evaluation	Randomisation and initial FS/FV application	Follow-up period (months)					
				6	12	18	24	30	36
Clinical data									
Medical/dental history/demographics	X				X		X		
Eligibility (inclusion/exclusion criteria)		X	X						
Caries risk-related habits			X		X		X		X
ICDAS caries assessment		X			X		X		X
Pre-treatment assessment ^a			X	X	X	X	X	X	
Adverse event assessment			X	X	X	X	X	X	X
Health economics data									
NHS resource usage interviews			X		X		X		X
Parental Resource Questionnaire			X		X		X		X
School Resource Questionnaire			X		X		X		X
Health-related quality of life (CHU-9D)					X		X		X
Treatment acceptability and process evaluation data									
Observational scale ^b			X	X	X	X	X	X	
DTF scale			X	X	X	X	X	X	
Interviews with children			X						X
Interviews with parents			X						X
Questionnaires/interviews with schools			X						X
Interviews with dental team ^c			X		X		X		X
Interviews with non-consenting parents	X	X	X						
Interviews with non-responding parent	X	X	X						
Interviews with withdrawing parents			d	d	d	d	d	d	d
CHU-9D, Child Health Utility Index 9D.									
a Assessment limited to condition of previously applied FS and/or pre-application risk assessment for FS/FV.									
b Completed by both dental hygienist and dental nurse during/immediately after treatment.									
c Dental team composed of dental officer, dental hygienist and dental nurse.									
d As required.									

Trial outcomes

Outcome measures for dental caries

The primary outcome measure was the development of dental caries on FPMs at 36 months. This was recorded as:

- the proportion of children developing new caries in dentine on any one of up to four treated FPMs at 36 months
- the number of treated FPM teeth that were free of caries into dentine at 36 months.

Outcome measures for health economic analysis

Indicators of clinical effectiveness were used alongside costs to estimate the relative cost-effectiveness of FS and FV.

Two additional outcome measures were used for the cost-effectiveness analysis. These were used to estimate incremental costs per quality-adjusted life-year (QALY) estimates.

Health-related quality of life: Child Health Utility Index 9D

A generic preference-based measure of health-related quality of life (HRQoL), the Child Health Utility Index 9D (CHU-9D),³⁰ was used to determine HRQoL. Designed specifically for use with children, the CHU-9D consists of a set of nine questions (dimensions), with five levels of responses available per question. It has a recall period of today/last night and is intended to be self-completed by the child (see *Appendix 14*).

Quality-adjusted tooth-years

Utility values were measured as quality-adjusted tooth-years (QATYs),^{31,32} which is the production of additional years of life (tooth-year) of each tooth adjusted for the quality of the tooth. An unrestored tooth has a QATY equal to 1 in the year it was restoration free, and a restored, crowned or root canal-treated tooth has a QATY of less than perfect (i.e. < 1) in the year that it was restored and in subsequent years. The QATY for an extracted tooth is equal to 0 in that year and in subsequent years. Data to inform the calculation of QATYs were derived from the clinical data collected.

Sample size

Data from a previous cohort study among primary school children under the care of the Cardiff and Vale UHB CDS were used to derive the caries incidence in children (mean age 6.5 years) with at least one erupted FPM.³³ Overall, 40% of children had caries in one or more of their FPMs by the age of 10 years. Based on recent Cochrane reviews, it is estimated that FV would reduce the 3-year incidence from 40% to 30% in this population,¹⁵ whereas FS would reduce it further to 20%.¹² For an individually randomised trial at a power of 80% with a significance level of 5%, at least 313 children per group were required for a comparison of caries incidence of 20% versus 30% at 36-month follow-up.

Randomisation

The randomisation of participants was stratified by school and balanced for sex and primary dentition baseline caries levels using minimisation in a 1 : 1 ratio for treatments. A random component was added to the minimisation algorithm,³⁴ such that it was not completely deterministic. The algorithm that allocated children to the study arm minimised imbalance with respect to sex and baseline caries levels, with a probability of 0.8 reducing the predictability of allocation.³⁵

Sequence generation

Randomisation was carried out in the South East Wales Trials Unit (SEWTU) using lists of pupil sex and caries chart data collected by the CDS from each school they visited for the screening examination. Eligible children were randomised using the minimisation algorithm. Allocation lists were produced and provided to the CDS, with a 2-week window before the CDS returned to the school for the baseline treatments.

Allocation concealment mechanism

All randomisation and allocation lists were produced by SEWTU independently of the recruiting and examining personnel in the CDS.

Implementation

The CDS carried out an initial screening examination at all schools. Data from these visits were provided to SEWTU and used to produce the allocation lists for the CDS. Allocations were provided to the CDS prior to each return school visit, ready for the children's baseline treatment.

Blinding

The physical nature of the technologies under test limited the scope for blinding. Both the participant and the dental hygienist were aware of the treatment provided. The dentist undertaking the clinical dental examinations at baseline and at 12, 24 and 36 months was not informed of the arm to which the participant had been randomised. However, the presence or absence of FS at assessment would obviously indicate the likely treatment received.

Statistical methods

All comparative analyses were carried out on an intention-to-treat basis (without imputation). The primary outcome (D_{4-6} MFT) was analysed using a logistic regression model to compare arms. The results for binary outcomes are presented as unadjusted and adjusted ORs for the FV arm compared with the FS arm (the reference arm). All models were adjusted for the randomisation balancing variables, sex and baseline caries, in the primary dentition. Baseline caries (decayed, missing, filled teeth in primary dentition, i.e. D_{4-6} MFT) was categorised as none, one or two, or three or more. The number of FPMs per child in the trial was also added to the models as a covariate but removed if non-significant. As the intervention was carried out within schools, a two-level logistic model was used to determine if there was any significant clustering by school. If clustering was found to be negligible, the primary analysis outcome was taken to be the single-level model. Intraclass correlation coefficients (ICCs) are given in tables or text for all two- and three-level models. For subgroup analyses, the appropriate addition of main effects and interaction terms was made to the primary model, as was the addition of any covariate effects.

For categorical outcomes with multiple categories, ordinal regression was fitted. The test of parallel lines was conducted to check that the assumption of proportional odds was satisfied. Count data were analysed using Poisson and negative binomial regression models. When the data were found to be overdispersed (greater variance than might be expected in a Poisson distribution), the negative binomial regression model was taken as the better-fitting model. When an inflation of zeros in the data was found, zero-inflated Poisson regression and zero-inflated negative binomial regression models were employed. The Akaike information criterion was used to determine the best-fitting model. The results were presented as adjusted incidence rate ratios in the FV arm compared with the FS arm.

For continuous outcomes, a linear regression model was fitted after transformation to normality, if required. When a natural log transformation was employed, the results were interpreted as percentage difference between the arms. When baseline measurements were taken into consideration, an analysis of covariance was used, with baseline measurement as a covariate. This model extends the usual logistic regression model to include correlated interim outcome data. It allows the main treatment effects to be adjusted for changes over time and for differences between time points to be examined. Differential changes over time in caries outcome between trial arms can be examined through the inclusion of a treatment \times time interaction term.

When data were collected over several time points, a repeated measures model (using a generalised logistic mixed model) was used with time points (12, 24 and 36 months). For tooth- and surface-level binary outcomes, two- and three-level logistic models were used when appropriate. An interaction term was used in the three-level models to investigate any differential effect of treatment on occlusal versus non-occlusal surfaces. For all primary and secondary outcomes, 95% CIs and p -values are presented.

Primary outcome calculation

The primary outcome was the proportion of children experiencing caries into dentine at ICDAS level 4–6 on any one of up to four FPMs in the trial at 36 months. The D_{4-6} MFT variable was calculated (and converted to a binary outcome) from the full caries charts of those children attending the 36-month examination and included only those FPMs in the trial. FPMs that were already sealed, carious into dentine, filled or affected by post-eruptive breakdown (PEB) at baseline were excluded from the trial.

Secondary outcomes calculation

Secondary caries models at child, tooth and surface levels were as follows:

- the number of FPMs remaining free of caries into dentine per child for those FPMs included in the trial (child-level ordinal analysis)
- the caries status of the FPMs (treated or untreated caries code 4, 5 or 6) included in the trial (tooth-level binary analysis)
- the number of surfaces on each FPM remaining dentine caries free per tooth within child for those FPMs included in the trial (tooth-level ordinal analysis)
- the caries status of treated or untreated caries on each surface of each FPM, caries code 4, 5 or 6 (surface-level binary analysis)
- the binary outcome of caries occurrence on occlusal versus non-occlusal surfaces of each FPM (surface-level binary analysis with an interaction term for surface type \times arm).

The primary analysis was undertaken using 12- and 24-month follow-up time points (child-level binary analyses). In addition, an investigation of the treatment differences on the earlier stages of caries development (enamel caries) was carried out using level 1, 2 and 3 of the ICDAS classification of caries at 36 months (child-level binary analysis). One additional post hoc analysis was carried out as a surface-level analysis of the binary outcome of all caries (ICDAS 1–6) with an interaction term for surface type to investigate occlusal versus non-occlusal surface interaction with treatment.

Treatment time

The treatment times at each time point were examined and found to be non-normally distributed. A natural log-transformation of the treatment time data was performed and a linear regression analysis was used to compare arms. Treatment effects are, therefore, interpreted as percentage difference between arms. The regression model was adjusted for the randomisation balancing variables sex and baseline caries.

Sealant retention

The sealant status at each treatment visit and the retention at each clinical examination were tabulated.

Molar incisor hypomineralisation

The presence and severity of MIH in the FPMs was tabulated at each dental examination, and the prevalence was reported by treatment arm. Severe MIH presenting with PEB at baseline excluded a FPM from the study.

Secondary analysis of primary outcomes

Additional important covariates were collected via the DHQ. The variables relating to tooth brushing frequency, toothpaste, mouthwash, fluoride tablets and fluoride drops were utilised in the primary model if there were ≥ 10 percentage points of difference between the binary categories. The variables relating to tooth brushing, amount of toothpaste and FV/gel applied were utilised in the primary model if there were ≥ 20 percentage points of difference between the binary categories. The following categorisations were used for covariates added to the primary analysis:

- frequency of tooth brushing – ‘twice or more a day’ versus ‘once or less a day’
- toothpaste type – ‘family toothpaste’ versus ‘children’s toothpaste or other’
- amount of toothpaste – ‘smear, pea or never’ versus ‘cover bristles’
- additional fluoride intake – ‘any mouthwash, drops or tablets or gel’ versus ‘none’.

Global oral hygiene regimen

A combined global rating scale of fluoride use and tooth brushing regimen was created as a summed score of the binary categories for tooth brushing frequency (twice a day); who carries out tooth brushing (adult or observed); toothpaste type (family toothpaste); amount of toothpaste (cover bristles); and additional fluoride (any yes response). This resulted in a score of 0–6, which was collapsed into four categories (0–1.49, 1.5–2.49, 2.5–3.49 and 3.5–6).

Length of time tooth brushing

The age of a child in months at baseline minus the age at which they started tooth brushing (in months) was converted to years (divided by 12). The distribution for length of time spent tooth brushing had slight negative skew but was entered into a linear regression untransformed.

Cariogenic score

The cariogenic score was calculated by summing the seven cariogenic items (scored 0–5) asked as part of the diet question in the DHQ (these items were c, d, e, g, h, k and m). At least four of these items had to be completed for a score to be calculated; if three or fewer of these items were ticked, the sugar intake score was set to missing. Following summation, the score was divided by (five times the number of completed items) and then multiplied by 100.

School and child deprivation

From the parental questionnaire, the child’s postcode was used to calculate the Welsh Index of Multiple Deprivation (WIMD) 2011.³⁶ The WIMD is categorised as quintiles and these were compared with the population of Wales as a whole. For analyses, the WIMD was trichotomised into categories 1–3, 4 or 5. The school postcode was coded in the same way and categorised as quintile for school-level analyses. School size was also tested in these two-level regression models.

Socioeconomic group

Parental occupation had five categories: ‘higher managerial, administrative and professional occupations’, ‘intermediate occupations’, ‘routine and manual occupations’, ‘unemployed’ and ‘homemaker, carer, student or grandparent’. These categories were based on those described by the Office for National Statistics.³⁷

Sensitivity analyses specific to primary outcomes

- Adjustment of the primary analysis for all treatments within the specified time window, 4 weeks either side of the scheduled treatment due date.
- The efficacy of the number of FV treatments on the primary outcome was estimated in a way that preserves randomisation using complier average causal effect (CACE) modelling. As-treated or per-protocol analyses have been widely used as secondary analyses if the effect of treatments when actually received is of interest. However, these secondary analysis methods may yield seriously biased estimates of treatment effects. Given the questionable validity of these analyses, statistical methods such as CACE estimation have been developed to better estimate treatment efficacy, taking into account non-compliance. The efficacy of the number of treatments on the primary outcome is estimated in a way that preserves randomisation. The structural mean model (SMM) approach for CACE was implemented here by fitting an instrumental variables regression. Applications of SMMs were developed to adjust for adherence in trials with active treatments and an untreated control arm. Although SoV has two active treatments, we have assumed, for the purposes of the CACE analysis, that the sealant is a one-off standard treatment comparable with a control arm, and so treatment visits were set to a constant zero. SoV also has a binary outcome, whereas CACE is more usually applied to linear outcomes. Hence, the standard instrumental variables regression in Stata® (version 13, StataCorp LP, College Station, TX, USA) was applied with the addition of robust standard errors. Adherence in the FV arm was defined as the number of FV treatment visits that a child attended (the instrumental variable) and the outputted estimate is interpreted as the efficacy per visit. A small, non-significant efficacy estimate indicates little effect of additional treatment visits and negligible adherence effects in the trial. Future work beyond the scope of this report will take these methods further and adjust for compliance, as well as for predictors of compliance in both arms.
- The SMM approach was implemented by fitting an instrumental variables regression.³⁸ Adherence was defined as the number of FV treatment visits that a child attended.

Subgroup analyses specific to primary outcome

Appropriate interaction terms were entered into the primary regression analysis in order to conduct prespecified subgroup analyses: cohort, baseline caries group. The trial was not powered to detect significant interactions and, as such, these analyses are exploratory only. ORs and 95% CIs were reported.

Imputation

Imputation was to be considered after an examination of the number of missing primary outcome data and the likely mechanism for missing data. If the primary outcome was deemed to be missing completely at random and the proportion of data missing for reasons other than moving out of the SoV area was less than 10%, then imputation would not be performed and a complete case analysis would be carried out to estimate an unbiased treatment effect. If differential dropout was observed between arms, this would indicate a missing at random or missing not at random mechanism. Mixed modelling is appropriate if the data are missing at random, whereas multiple imputation and associated sensitivity analyses may be more appropriate if the missing data were determined to be missing not at random.

Reliability

Calibration of the dental examiners was carried out each year of the study, and kappa scores were calculated for reliability. At each clinical examination, a 5% sample was re-examined and caries charts were completed a second time.

Statistical software employed

All analyses were carried out in IBM SPSS Statistics version 20 (IBM Corporation, Armonk, NY, USA), except the zero-inflated Poisson regression, zero-inflated negative binomial regression and *ivregress* (CACE) models, which were carried out in Stata.

Assessment of adverse effects

During the course of the study, the occurrence of any serious adverse events or serious adverse reactions was ascertained and recorded using the study serious adverse events form (see *Appendix 15*).

As per the Design to Smile programme, the clinical staff involved in the delivery of the intervention monitored participants during and immediately following the administration of FS or FV, and were available to manage any adverse events or serious adverse reactions in accordance with current clinical practice.

Parents were asked to tell the CDS team if their child experienced any dental or medical problems during the 48 hours after each treatment.

Design of study materials and strategy for maximising questionnaire follow-up rates

Participant information sheet

As described in section 4.8 of the ICH *Guideline for Good Clinical Practice*,²³ in order that research participants (or their legal guardians) are able to make an informed decision on whether or not to take part in a clinical trial, all relevant information must be provided to the participants in such a way that it is as non-technical and understandable as possible.

With this in mind, it was essential that all participant materials (including the PIS) were developed taking into consideration the diverse literacy levels of the target population (i.e. parents of children in Communities First areas).

To achieve this, the PIS was developed in consultation with a parents' group in Newport. This group is in a Communities First area of South Wales but one that is not served by the Cardiff and Vale CDS; therefore, it was not within the catchment area of the trial.

After the initial draft by the SoV project team, the PIS and consent form were reviewed by the parents' group, and the following points that they made were taken into account for subsequent revisions.

- All of the parents agreed that the overall amount of information/text presented was too extensive and would be very likely to discourage them from thoroughly reading the information sheet (if they read it at all). Furthermore, they felt that the tone of the wording needed to be made more 'positive'. Once the parents had had time to digest the information and understand the study, they agreed that it was a 'positive' thing and would want their children to participate if a similar study was run in their area.
- Parents felt that having separate information sheets for parents and children was unnecessary, and that it would be easier for parents to be given one simplified information sheet, which they could use to discuss the study with their child. Parents felt that the wording used in the information sheet for children was much more accessible and that the one simplified information sheet should contain wording more similar to this.
- Parents showed a strong aversion to the word 'research' being used (the image of children being used as 'guinea pigs' was expressed by several parents). They felt that 'evaluation' or 'assessment' conveyed the same concept in a more acceptable and understandable way.
- The use of cartoons/graphics/photographs was encouraged.
- Parents felt that the duplication of wording in the information sheet and the consent form was unnecessary, and that cross-referencing should be used to help the parents understand better which items on the consent form referred to which parts of the PIS.

Despite considering the recommendations of the parents' group, we were mindful of the guidance provided in section 4.8.10 of ICH topic E 6 (*Guideline for Good Clinical Practice*²³), and tried to convey to those in the group that a minimum level of information was required when developing an information

sheet for a clinical trial of an investigational medicinal product (CTIMP). The revised PIS was therefore intended to represent a risk-based approach to the information provided to parents for a CTIMP.

In addition to ensuring that the content of the PIS was suitable, the visual appeal of the document was further developed by a graphic designer, incorporating the child-friendly logos and colour schemes of the CDS.

Follow-up questionnaires: development and return rate

Information relating to caries risk-related habits and parental resource utilisation was obtained from parents via a single combined DHQ (see *Appendix 13*) at baseline and at 12, 24 and 36 months. This was accompanied (at the 12-, 24- and 36-month time points only) by the CHU-9D (see *Appendix 14*), both of which were distributed to participants' homes at the required time points.

The initial return rates of these questionnaires were lower than expected. The initial follow-up strategy allowed for one follow-up telephone call 2 weeks after the questionnaires were handed out. However, unanswered calls and inactive numbers made this strategy ineffective.

Initially, a £5 shopping voucher was included with the questionnaires in an effort to boost return rates, but responses remained poor, with an overall return rate of 53%. A consultation exercise followed with parents of children at a primary school in a Communities First area not involved in the trial. Between this consultation and ideas developed by the trial management group, the following changes to the strategy for follow-up of questionnaires were made.

- The questionnaire pack was to be given to the child at treatment/examination.
- A trial-branded giveaway (pen, eraser or fridge magnet) was included.
- A text message reminder was sent if the questionnaire was not returned 1 week after distribution.
- A second copy of the questionnaire was sent to participants' homes if the original was not received 2 weeks after distribution.
- A telephone call was made directly to parents to remind them/aid with questionnaire completion (DHQ only) and return.
- Participants were informed that all returned questionnaires gained entry to a prize draw for an iPad® (Apple Inc., Cupertino, CA, USA) at each time point.
- The questionnaires were reformatted to increase their visual appeal, and were designed to be consistent with the PIS and ICF, using the colours and graphics of the Designed to Smile programme.

Patient and public involvement

Patient and public involvement (PPI) in the SoV trial has been utilised in two main ways. The first has been described in previous sections regarding the development of the study materials with the help of members of a parents' group in Newport. This PPI input was pivotal in producing user-friendly materials, contributing to the successful recruitment to target. Without this detailed input, we would not have been able to justify the carefully judged brevity and clarity of the PIS to the REC.

The second major use of PPI was in the redesign of participant-facing materials, as described in *Design of study materials and strategy for maximising questionnaire follow-up rates*. This helped to boost the return rate of follow-up questionnaires, thereby increasing our overall data collection.

Patient and public involvement was maintained throughout the trial via lay member representation on the Trial Steering Committee (TSC). Our TSC lay member is a member of the Involving People network, a Welsh Government-funded organisation that promotes PPI in research across Wales. The contribution of this member to TSC meetings was invaluable, bringing a lay perspective to deliberations.

Health economic assessment

A health economic evaluation was conducted alongside the trial. The evaluation set out to:

- estimate the costs of providing FS versus FV and the outcomes for the NHS, children and their families and education in order to consider a partial societal perspective
- establish the relative cost-effectiveness of FS versus FV
- calculate the budget impact on the NHS of FS and FV delivered in a community/school setting.

The costs associated with the interventions for each trial participant were collected and summarised into the following categories:

- Implementation costs of the interventions.
- Health-care utilisation costs associated with travel or caregiving/time of work for families.
- Costs associated with the schools, for example as a result of child absence. Published unit costs were used or, when unavailable, local financial records were used to value resources in monetary terms using 2015 as the price year.

A series of within-trial incremental cost-effectiveness ratios (ICERs) were calculated (based on a NHS perspective) to estimate the cost per:

- caries increment avoided
- QALY, using the CHU-9D to derive health utilities
- QATY as an exploratory analysis.

Post-trial modelling was conducted to estimate the longer-term cost-effectiveness of the interventions. One-way sensitivity analysis was undertaken to assess the impact on changes to individual parameters on the base-case results with probabilistic sensitivity analysis undertaken to estimate the joint uncertainty around parameters. A budget impact analysis was undertaken to estimate the impact on NHS budgets in delivering the interventions. A detailed report on the health economic methods is provided in *Chapter 4*.

Treatment acceptability assessment and process evaluation

Treatment acceptability was assessed in three ways:

1. acceptability scales were completed by clinical staff
2. acceptability scales were also completed by the children participating in the trial
3. qualitative interviews were conducted with a subsample of children.

The treatment acceptability scales and the qualitative interviews are described in *Chapter 5*.

Chapter 3 Clinical results

This chapter describes the clinical findings of the trial.

Introduction

The chapter begins with a description of the number of children randomised to the trial, and a Consolidated Standards of Reporting Trials (CONSORT) diagram³⁹ describes participant flow through the trial. The baseline characteristics of the participants are described in relation to trial arm and to those starting, completing and failing to complete the trial. Next, potential confounding factors such as fluoride exposure, diet and dental attendance are reported. Participation and retention data are also described.

The main clinical results of the study in relation to the primary outcome measure, the proportion of children developing caries into dentine on any treated FPM, are reported. The impact of baseline caries experience, school attended, deprivation status and trial cohort is examined, before the impact of oral hygiene habits, diet and dental attendance is analysed.

The second main trial outcome, the number of teeth developing dentine caries (D₄₋₆MFT) at 36 months, is reported next at both tooth and tooth-surface level. Fidelity is then described using CACE analysis. Compliance with treatment windows is also reported.

The effect of including enamel caries (D₁₋₆MFT) in the analysis is then described. This is followed by examining the impact of the FS and FV treatments on all permanent teeth, not only FPMs. Trial outcomes at 12 and 24 months are reported to illustrate the shorter-term impact of the trial interventions. Finally, the following data are presented: sealant retention, examiner reproducibility, adverse effects and treatment time.

Participant screening for participation in the trial

In total, 1303 children for whom parental consent had been obtained were screened for participation in the trial (*Figure 2*). Of these, 1016 were deemed eligible for inclusion, but one participant subsequently withdrew consent for participation and for the use of any of their data. At screening, 287 children were excluded. The participants were recruited in two cohorts between October and January in the school years 2011/12 and 2012/13.

Participant randomisation

Participants were randomised to receive FS (514 children) or FV (501 children), as described in *Chapter 2*.

Characteristics of included participants at baseline

The characteristics of the study participants who were randomised at baseline are shown in *Table 3*. There were no apparent differences between trial arms in sex or in the proportion of children with caries experience in their primary dentition. The high prevalence of dental caries experienced in the primary dentition at baseline (54.1%) reflects the fact that the programme was specifically targeted at schools in areas of high social and economic deprivation. As shown in *Figure 3*, 78.6% of children randomised lived in the bottom two quintiles of deprivation in Wales. Within quintiles of deprivation, the distribution of children across trial arms was broadly similar.

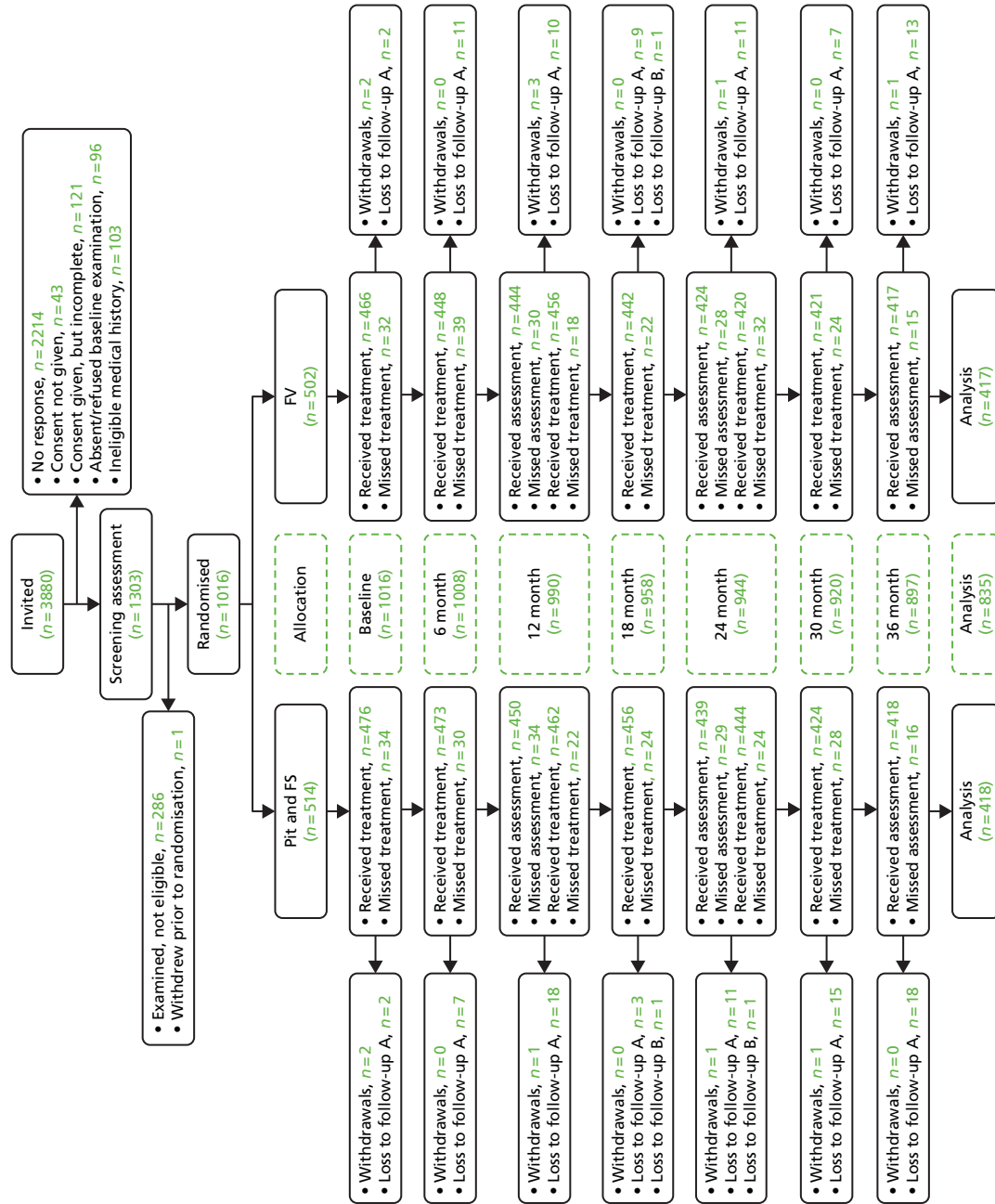
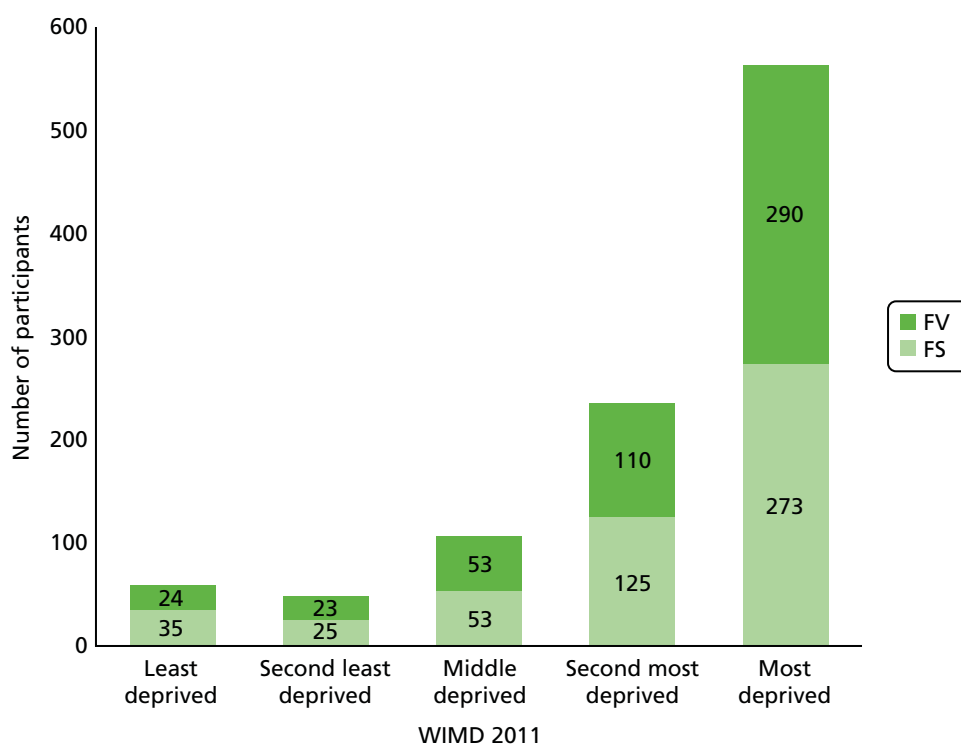


FIGURE 2 The CONSORT diagram of participant flow through the trial. One participant from the FV arm subsequently withdrew consent to use all data. Loss to follow-up A, moved to a non-participating school; loss to follow-up B, change in medical circumstances prevented further participation in the trial.

TABLE 3 Characteristics at baseline of the 1015 children randomised to participate in the trial

Characteristic	Intervention arm		Total, n (%)
	FS, n (%)	FV, n (%)	
Children randomised	514 (50.6)	501 (49.4)	1015 (100)
Sex			
Male	237 (46.1)	235 (46.9)	472 (46.5)
Female	277 (53.9)	266 (53.1)	543 (53.5)
Children with dentine caries in the primary dentition (d_{4-6})	286 (55.6)	266 (53.1)	552 (54.1)
Children with dentine caries in the primary dentition (d_{4-6} mft)	342 (66.5)	339 (67.7)	681 (67.1)
Children with untreated dentine caries in any FPM (D_{4-6})	22 (4.3)	23 (4.6)	45 (4.4)
Children with dentine caries in any FPM (D_{4-6} MFT)	27 (5.3)	31 (6.2)	58 (5.7)
d_{4-6} mft, mean (SD)	3.2 (3.4)	3.2 (3.3)	3.2 (3.3)
d_{1-6} mft, mean (SD)	4.6 (3.8)	4.6 (3.7)	4.6 (3.7)
d_{4-6} mfs, mean (SD)	8.9 (12.3)	9.6 (12.4)	9.3 (12.3)
d_{1-6} mfs, mean (SD)	11.0 (12.9)	11.6 (12.9)	11.3 (12.9)

dmfs, decayed, missing, filled tooth surfaces in primary dentition; SD, standard deviation.

**FIGURE 3** Social and economic profile of trial participants at baseline by trial arm and by quintile of WIMD (2011).

The characteristics at baseline of the 835 children who completed the trial and of the 180 children who either were lost to follow-up or withdrew are shown in *Tables 4* and *5*. There were no marked differences in the baseline characteristics of either of these groups in relation to dental caries experience at baseline.

TABLE 4 Characteristics at baseline of the 835 children who were examined at 36 months

Characteristic	Intervention arm		Total, n (%)
	FS, n (%)	FV, n (%)	
Children completing the trial	418 (50.1)	417 (49.9)	835 (100)
Sex			
Male	193 (46.2)	196 (47.0)	389 (46.6)
Female	225 (53.8)	221 (53.0)	446 (53.4)
Children with dentine caries in the primary dentition (d_{4-6})	228 (54.5)	219 (52.5)	447 (53.5)
Children with dentine caries in the primary dentition (d_{4-6} mft)	271 (64.8)	280 (67.1)	551 (66.0)
Children with untreated dentine caries in any FPM (D_{4-6})	16 (3.8)	17 (4.1)	33 (4.0)
Children with dentine caries in any FPM (D_{4-6} MFT)	18 (4.3)	24 (5.8)	42 (5.0)
d_{4-6} mft, mean (SD)	3.1 (3.4)	3.2 (3.3)	3.2 (3.4)
d_{1-6} mft, mean (SD)	4.5 (3.7)	4.6 (3.7)	4.5 (3.7)
d_{4-6} mfs, mean (SD)	8.8 (12.4)	9.7 (12.7)	9.3 (12.5)
d_{1-6} mfs, mean (SD)	10.9 (12.9)	11.7 (13.2)	11.3 (13.1)

dmfs, decayed, missing, filled tooth surfaces in primary dentition; SD, standard deviation.

TABLE 5 Characteristics at baseline of the 180 children who were lost to follow-up or withdrew from the trial

Characteristic	Intervention arm		Total, n (%)
	FS, n (%)	FV, n (%)	
Children randomised	96 (53.3)	84 (46.7)	180 (100)
Sex			
Male	44 (45.8)	39 (46.4)	83 (46.1)
Female	52 (54.2)	45 (53.6)	97 (53.9)
Children with dentine caries in the primary dentition (d_{4-6})	58 (60.4)	47 (56.0)	105 (58.3)
Children with dentine caries in the primary dentition (d_{4-6} mft)	71 (74.0)	59 (70.2)	130 (72.2)
Children with untreated dentine caries in any FPM (D_{4-6})	6 (6.2)	6 (7.1)	12 (6.7)
Children with dentine caries in any FPM (D_{4-6} MFT)	9 (9.4)	7 (8.3)	16 (8.9)
d_{4-6} mft, mean (SD)	3.4 (3.3)	3.3 (3.1)	3.4 (3.2)
d_{1-6} mft, mean (SD)	4.8 (3.9)	4.7 (3.4)	4.8 (3.6)
d_{4-6} mfs, mean (SD)	9.5 (11.8)	9.2 (11.2)	9.4 (11.5)
d_{1-6} mfs, mean (SD)	11.7 (12.9)	11.3 (11.5)	11.5 (12.3)

dmfs, decayed, missing, filled tooth surfaces in primary dentition; SD, standard deviation.

Characteristics of first permanent molars in children randomised to the trial

The status of the FPMs by quadrant is shown in *Table 6*. From this, it is apparent that the prevalence of decay into dentine was very low at baseline, the D_{4-6} MFT ranging from 1.2% of upper-right permanent first molars to 2.9% of lower-right FPMs. A greater proportion of upper FPMs (9.2–9.4%) were unerupted than lower FPMs (4.7–5.9%). The percentage of erupted (or partially erupted) FPMs that were free of caries into dentine was recorded as 89.7% in the upper-right quadrant and 93.5% in the lower-right quadrant.

With 1015 children randomised to participate in the trial and assessed at baseline, the overall number of FPMs was 4060. In total, 161 (4%) of these were excluded at baseline because of the presence of FS (71 teeth), caries into dentine (56 teeth), filled teeth (17 teeth) and teeth with PEB (17 teeth) (*Table 7*).

Baseline characteristics: fluoride exposure, diet and dental attendance

A questionnaire distributed to the participants' parents was used to collect information on exposure to fluoride, dietary intake and dental attendance. At the baseline examination, 597 questionnaires were returned, representing 58.8% of the study participants.

Fluoride exposure

From *Table 8*, it is apparent that the arms were reasonably well matched in terms of reported exposure to fluoride outside the trial interventions. Reported tooth brushing frequency was higher in the FV group, with 74.6% claiming twice-daily brushing, compared with 68.5% in the sealant group.

TABLE 6 The status of FPMs by quadrant at baseline for the 1015 children randomised to the trial

Status	FPM			
	UR ($N = 1015$), n (%)	UL ($N = 1015$), n (%)	LR ($N = 1015$), n (%)	LL ($N = 1015$), n (%)
Unerupted	93 (9.2)	95 (9.4)	60 (5.9)	48 (4.7)
D_{1-3} T	114 (11.2)	120 (11.8)	109 (10.7)	107 (10.5)
D_{4-6} T	11 (1.1)	10 (1.0)	24 (2.4)	12 (1.2)
MT	0 (0)	0 (0)	0 (0)	0 (0)
FT	1 (0.1)	5 (0.5)	5 (0.5)	5 (0.5)
D_{1-3} MFT	115 (11.3)	125 (12.4)	114 (11.2)	112 (11.0)
D_{4-6} MFT	12 (1.2)	15 (1.5)	29 (2.9)	17 (1.7)
D_{1-3} S	115 (11.3)	123 (12.1)	114 (11.2)	111 (10.9)
D_{4-6} S	11 (1.1)	10 (1.0)	24 (2.4)	12 (1.2)
MS	0 (0)	0 (0)	0 (0)	0 (0)
FS	1 (0.1)	6 (0.6)	5 (0.5)	5 (0.5)
D_{1-3} MFS	116 (11.4)	128 (12.6)	118 (11.6)	116 (11.4)
D_{4-6} MFS	12 (1.2)	15 (1.5)	29 (2.9)	17 (1.7)
Free of caries (D_{1-6} MFT = 0)	796 (78.4)	785 (77.3)	817 (80.5)	843 (83.1)
Free of caries into dentine (D_{4-6} MFT = 0)	910 (89.7)	905 (89.2)	926 (91.3)	950 (93.5)

FT, filled tooth; LL, lower left; LR, lower right; UL, upper left; UR, upper right.

TABLE 7 The distribution of FPMs included and excluded from the trial, together with reasons for exclusion

	FPM								Total (N = 4060)	
	UR (N = 1015)		UL (N = 1015)		LR (N = 1015)		LL (N = 1015)			
	n	%	n	%	n	%	n	%	n	%
Teeth included	978	96.4	983	96.8	962	94.8	976	96.2	3899	96.0
Teeth excluded	37	3.6	32	32.2	53	5.2	39	3.8	161	4.0
Reason for exclusion (n, % excluded)										
Sealed	20	54.1	14	43.8	20	37.7	17	43.6	71	44.1
Filled	1	2.7	6	18.8	5	9.4	5	12.8	17	10.5
Caries at into dentine (D ₄₋₆)	11	29.7	9	28.1	24	45.3	12	30.8	56	34.9
PEB ^a	5	13.5	3	9.4	4	7.5	5	12.8	17	10.5

LL, lower left; LR, lower right; UL, upper left; UR, upper right.

^a The PEB category is not necessarily mutually exclusive of other categories.

TABLE 8 Reported exposure to fluoride at baseline by intervention arm

Variable	Scoring	FS (N = 314), n (%)	FV (N = 283), n (%)	Total (N = 597), n (%)
Frequency of tooth brushing	Never	0 (0.0)	0 (0.0)	0 (0.0)
	Less than once a day	4 (1.3)	4 (1.4)	8 (1.4)
	Once a day	77 (25.0)	48 (17.4)	125 (21.4)
	Twice a day	221 (68.5)	206 (74.6)	417 (71.4)
	More than twice a day	16 (5.2)	18 (6.5)	34 (5.8)
Toothpaste type	Family toothpaste	168 (55.3)	134 (48.9)	302 (52.2)
	Children's toothpaste	131 (43.1)	133 (48.5)	264 (45.7)
	Other	5 (1.6)	7 (2.6)	12 (2.1)
Amount of toothpaste	A smear	24 (7.8)	23 (8.3)	47 (8.0)
	A pea-sized amount	250 (81.4)	222 (80.1)	472 (80.8)
	Cover the bristles	33 (10.7)	32 (11.6)	65 (11.1)
Use of mouthwash		97 (32.1)	82 (30.3)	179 (31.2)
Use of fluoride tablets		2 (0.9)	0 (0.0)	2 (0.5)
Use of fluoride drops		0 (0.0)	0 (0.0)	0 (0.0)
Use of FV		51 (16.6)	35 (12.6)	86 (14.7)
Lifetime resident in South Wales		238 (90.8)	215 (91.9)	453 (91.3)

A greater proportion (55.3%) of parents in the FS arm than in the FV arm (48.9%) reported that their child used family toothpaste to clean their teeth. The amount of toothpaste used on toothbrushes was broadly similar between the trial arms. In both trial arms, 91% of the participants were lifetime residents of non-fluoridated South Wales.

Global oral hygiene regimen

The combined global rating scale of fluoride use and tooth brushing regimen, calculated as described in *Chapter 2*, is shown in *Table 9*. This shows that the global oral hygiene score increased in both trial arms from baseline to 12 months and was marginally higher in the FV arm than in the FS arm at 12, 24 and 36 months.

Diet

Reported dietary intake at baseline is shown in *Table 10* and summarised in *Table 11*.

Cariogenic score

The cariogenic score, derived as described in *Chapter 2*, gives a summary measure of exposure to cariogenic dietary items and is reported in *Table 11*. This shows that, although the score reduced between the baseline and the 12-month examinations, it remained relatively constant thereafter and differed little between the intervention arms.

Dental attendance

On the topic of dental attendance, 92.6% of children in the FS arm and 90.9% of children in the FV arm were reported as being regular dental attenders, with the remainder described by their parents as attending only when they were in pain.

Participation and retention

Of the 1016 children randomised to the trial, 835 (82.2%) underwent a final clinical examination at 36 months. The number completing the FS arm was 418 and the number completing the FV arm was 417. The most common reason that children did not complete the trial was that they had moved away from the area or to a school that was not participating in the trial; this was reported as lost to follow-up (see *Figure 2*). The number of children who withdrew from the trial was five in the FS arm and seven in the FV arm.

It can be seen from the CONSORT diagram (see *Figure 2*) that the proportion of missing primary outcome in each arm is evenly distributed by reason. Only 21 out of 514 (4.1%) participants in the FS arm and 22 out of 502 (4.4%) participants in the FV arm were a result of absence on the day of the final examination or study withdrawal. Missing data attributable to participants moving out of the SoV area and a change in medical circumstances were deemed to be unrelated to the treatments and, therefore, a completely random mechanism. Moreover, the number of missing data that may possibly be related to treatment was very low; therefore, imputation was not carried out and a complete case analysis is appropriate. Estimates or treatment effect from these analyses will be unbiased with regard to missing data.

TABLE 9 Global oral hygiene regimen: summary score of reported oral hygiene habits during the trial by intervention arm

	Intervention					
	FS		FV		Overall	
	<i>n</i>	Mean (SD)	<i>n</i>	Mean (SD)	<i>n</i>	Mean (SD)
Global oral hygiene regimen						
Baseline	309	2.50 (1.083)	280	2.47 (1.018)	589	2.49 (1.052)
12 months	296	2.72 (1.136)	270	2.81 (1.183)	566	2.76 (1.159)
24 months	312	2.71 (1.204)	292	2.78 (1.130)	604	2.74 (1.169)
36 months	269	2.70 (1.035)	254	2.83 (1.090)	523	2.76 (1.063)

SD, standard deviation.

TABLE 10 Reported dietary intake at baseline by intervention arm

Variable	Scoring	Intervention arm		Total, n (%)
		FS, n (%)	FV, n (%)	
Milk	Never and up to 4–6 times per week	102 (33.6)	93 (34.1)	195 (33.8)
	1 per day to 2–3 times per day	202 (66.4)	180 (65.9)	382 (66.2)
Water	Never and up to 4–6 times per week	88 (29.4)	69 (25.3)	157 (27.4)
	1 per day to 2–3 times per day	211 (70.6)	204 (74.7)	415 (72.6)
Fizzy drinks	Never and up to 4–6 times per week	264 (88.6)	233 (87.3)	497 (88.0)
	1 per day to 2–3 times per day	34 (11.4)	34 (12.7)	68 (12.0)
Squash	Never and up to 4–6 times per week	174 (60.0)	135 (51.5)	309 (56.0)
	1 per day to 2–3 times per day	116 (40.0)	127 (48.5)	243 (44.0)
Fruit juice	Never and up to 4–6 times per week	210 (72.2)	186 (70.3)	395 (71.3)
	1 per day to 2–3 times per day	81 (27.8)	78 (29.7)	159 (28.7)
Diet/light drinks	Never and up to 4–6 times per week	202 (69.9)	167 (63.5)	369 (66.8)
	1 per day to 2–3 times per day	87 (30.1)	96 (36.5)	183 (33.2)
Sweets/confectionery	Never and up to 4–6 times per week	236 (77.4)	214 (79.6)	450 (78.4)
	1 per day to 2–3 times per day	69 (22.6)	55 (20.4)	124 (21.6)
Chocolate	Never and up to 4–6 times per week	242 (79.1)	214 (79.3)	456 (79.2)
	1 per day to 2–3 times per day	64 (20.9)	56 (20.7)	120 (20.8)
Crisps	Never and up to 4–6 times per week	235 (76.5)	205 (75.9)	440 (76.3)
	1 per day to 2–3 times per day	72 (23.5)	65 (24.1)	137 (23.7)
Fruit	Never and up to 4–6 times per week	93 (30.5)	67 (24.6)	160 (27.7)
	1 per day to 2–3 times per day	212 (69.5)	205 (75.4)	417 (72.3)
Biscuits and cakes	Never and up to 4–6 times per week	231 (75.7)	210 (76.9)	441 (76.3)
	1 per day to 2–3 times per day	74 (24.3)	63 (23.1)	137 (23.7)
High-fibre cereals	Never and up to 4–6 times per week	189 (62.0)	159 (58.5)	348 (60.3)
	1 per day to 2–3 times per day	116 (38.0)	113 (41.5)	229 (39.7)
Other cereals	Never and up to 4–6 times per week	220 (73.1)	192 (71.1)	412 (72.2)
	1 per day to 2–3 times per day	81 (26.9)	78 (28.9)	159 (27.8)

TABLE 11 Cariogenic score: summary score of reported dietary habits during the trial by intervention arm

	Intervention arm					
	FS		FV		Overall	
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
Cariogenic score						
Baseline	307	45.079 (15.3528)	275	46.188 (14.3435)	582	45.603 (14.8820)
12 months	299	44.997 (16.3388)	268	43.996 (14.5916)	567	44.524 (15.5320)
24 months	308	43.929 (14.2771)	289	43.053 (14.1149)	597	43.505 (14.1936)
36 months	266	42.097 (14.1395)	254	42.980 (14.5780)	520	42.528 (14.3483)

SD, standard deviation.

The number of children who missed treatment at each of the 6-month intervals was small; for example, at the 12-month treatment session, 22 out of 484 (4.5%) missed treatment in the FS arm, and the corresponding figure in the FV arm was 18 out of 474 (3.8%). This was because the children had been absent from school on the day the MDC visited. As shown in *Table 12*, in both arms of the study 95% of participants received the treatment on five or six of the six scheduled treatment visits, indicating extremely high fidelity in the study.

At the final assessment (36 months), the clinical team visited the schools on a second occasion to pick up any absentees. Of the 866 children remaining in the trial and eligible for clinical assessment, 835 (94.6%) were examined.

Participation rates across the trial by arm and by assessment and treatment visits are shown in *Figure 4*. It is clear that, although there was a gradual loss of participants throughout the trial, the loss was equal

TABLE 12 Number of individual treatment visits by arm

Treatment visits attended	Intervention arm, <i>n</i> (%)	
	FS (<i>N</i> = 418)	FV (<i>N</i> = 417)
0	0 (0)	0 (0)
1	1 (0.2)	0 (0)
2	0 (0)	1 (0.2)
3	2 (0.5)	4 (1.0)
4	16 (3.8)	15 (3.6)
5	92 (22.0)	96 (23.0)
6	307 (73.4)	301 (72.2)

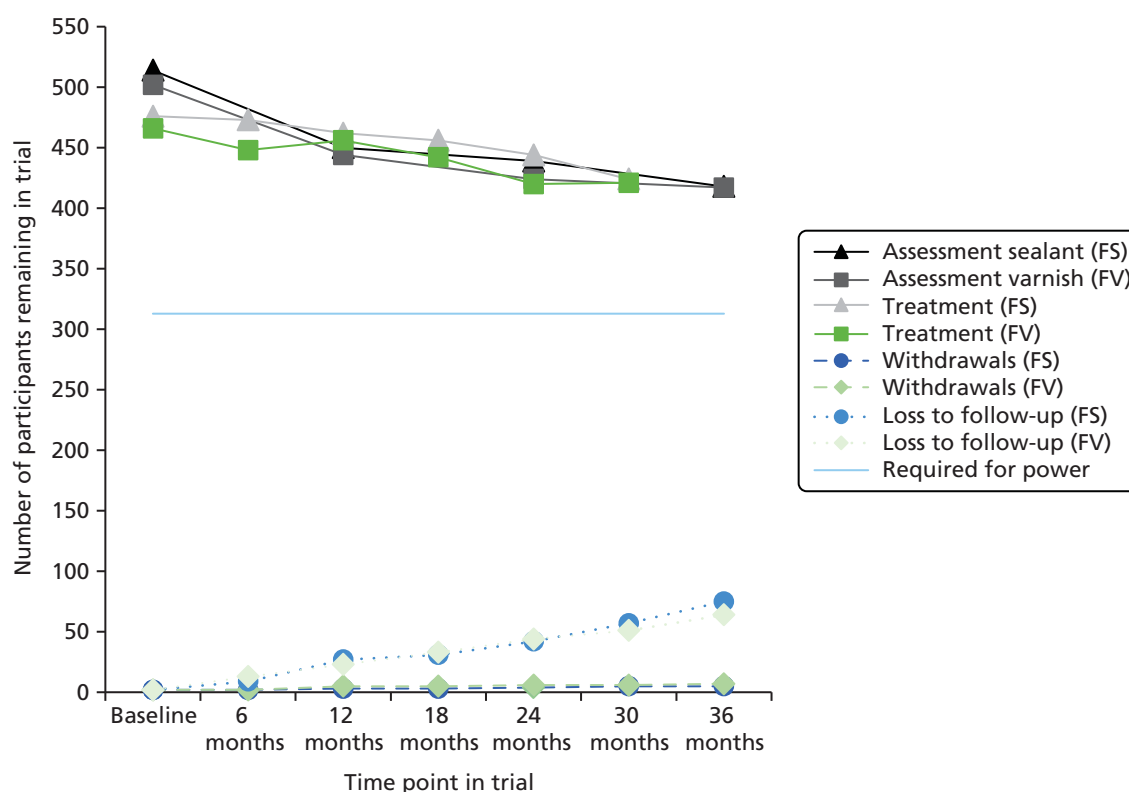


FIGURE 4 Participation rates across the trial by arms and by assessment and treatment visits.

between the arms, and numbers of children remaining, at 418 and 417, were well in excess of the required 313 per arm as determined in the power calculation (see *Chapter 2, Sample size*).

Clinical results

The proportion of children developing caries into dentine, having a restoration or extraction on at least one first permanent molar at 36 months

The primary outcome measure of the trial was the proportion of children developing new caries into dentine on any one of up to four treated FPMs (*Table 13* and *Figure 5*). The proportion of children with dentine caries (D₄₋₆MFT) on any one of their FPMs was compared between those who had sealant and those who had FV.

The proportion of children who developed dentine caries (D₄₋₆MFT) on at least one FPM at 36 months was broadly similar in the FS (19.6%) and the FV (17.5%) arms.

The OR for developing caries in the FV arm (when compared with the FS arm) was 0.87 (95% CI 0.61 to 1.23) in the unadjusted model, that is, children who received FV were slightly less likely to develop caries than those who received FS, but the difference was not statistically significant (*Table 14*).

TABLE 13 The proportion of children with dentine caries (D₄₋₆MFT) on any FPM in the trial at 36-month follow-up by trial arm

	Intervention arm, n (%)		
	FS (N = 418)	FV (N = 417)	Total (N = 835), n (%)
No dentine caries on any FPM	336 (80.4)	344 (82.5)	680 (81.4)
Dentine caries (D ₄₋₆ MFT) on at least one FPM	82 (19.6)	73 (17.5)	155 (18.6)

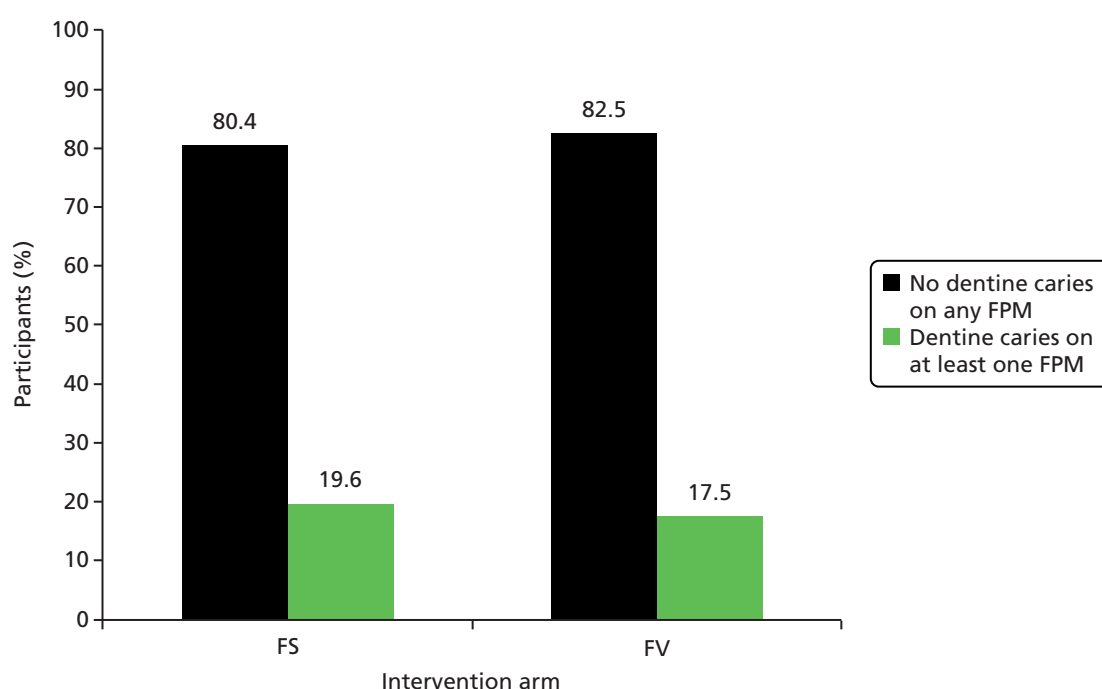


FIGURE 5 The proportion of children with dentine caries (D₄₋₆MFT) on any FPM in the trial at 36-month follow-up by trial arm.

TABLE 14 Primary analysis of the proportion of children with dentine caries, a restoration or extraction (D₄₋₆MFT) on any FPM in the trial by trial arm at 36 months

	Unadjusted OR (95% CI)	p-value	Adjusted ^a OR (95% CI)	p-value
FS	Reference		Reference	
FV	0.87 (0.61 to 1.23)	0.433	0.84 (0.59 to 1.21)	0.351
Baseline caries prevalence				
Primary dentition free of caries into dentine			Reference	
1–2 primary teeth with caries into dentine			1.58 (0.83 to 3.00)	0.165
≥ 3 primary teeth with caries into dentine			4.57 (2.83 to 7.39)	< 0.001
Sex				
Female			Reference	
Male			1.06 (0.74 to 1.52)	0.756

a FV compared with FS. Analysis adjusted for baseline caries prevalence and sex.

As sex and baseline caries prevalence were used to balance the randomisation, an adjusted model was also performed, and this was taken as the primary analysis. The OR for developing caries in the FV arm was 0.84 (95% CI 0.59 to 1.21) in the adjusted model.

In summary, the final model (see *Table 14*) shows that there was no significant difference in the proportion of children with dentine caries (D₄₋₆MFT) on any FPM in the trial at 36 months regardless of whether the children received FS or FV. Children who had more than three carious primary teeth at baseline were significantly more likely to develop caries into dentine on a FPM at 36 months. There was no difference between the proportion of boys and girls developing caries into dentine on at least one FPM.

The influence of treating dental hygienist

Two trained experienced dental hygienists delivered the intervention. When the treating hygienist at baseline was added to the single-level primary analysis as a factor, this was not significant ($p = 0.981$) and did not change the primary outcome. When the primary outcome was modelled adjusted for treating hygienist using a two-level logistic regression model, the outcome was unchanged compared with the unadjusted result. The ICC for hygienist was zero, and so there was no clustering by staff delivering the intervention.

The influence of school attended

To determine if there was any clustering in the primary outcome at school level, a two-level multilevel logistic regression was carried out. The results from the two-level model did not differ from the primary model to any significant degree (*Table 15*) and school was dropped as level for subsequent analyses. The ICC for school was 0.029 in the unadjusted model and 0.024 in the adjusted model.

The influence of cohort and baseline caries experience

To examine the influence of two prespecified subgroups on the primary outcome, an exploratory analysis was undertaken. The children were recruited to the trial in two cohorts (see *Chapters 2 and 6*) over two school years. The purpose of this analysis was to examine whether or not there were significant differences in the primary outcome measures between the trial cohorts. The second analysis examined the effect of caries in the primary dentition at the baseline examination on subsequent development of caries on FPMs. The number of children developing D₄₋₆MFT at 36 months related to the trial cohort and to the number of decayed primary teeth at baseline is shown in *Table 16*.

CLINICAL RESULTS

TABLE 15 Analysis of the proportion of children with dentine caries, a restoration or tooth extracted because of caries (D₄₋₆MFT) on any FPM in the trial by trial arm at 36 months, adjusted for school attended

	Unadjusted OR (95% CI)	p-value	Adjusted ^a OR (95% CI)	p-value
FS	Reference		Reference	
FV	0.87 (0.61 to 1.23)	0.426	0.84 (0.59 to 1.21)	0.358
Baseline caries				
Primary dentition free of caries into dentine			Reference	
1–2 primary teeth with caries into dentine			1.61 (0.84 to 3.07)	0.150
≥ 3 primary teeth with caries into dentine			4.56 (2.81 to 7.40)	< 0.001
Sex				
Female			Reference	
Male			1.06 (0.74 to 1.53)	0.747

a FV compared with FS. Analysis adjusted for baseline caries prevalence and sex.

TABLE 16 The development of dentine caries (D₄₋₆MFT) on any FPM at 36 months by cohort and baseline caries experience in the primary dentition at baseline

	Intervention arm, n (%)		Total (N = 835), n (%)
	FS (N = 418)	FV (N = 417)	
No dentine caries in FPMs at 36 months			
Cohort 1	173 (51.5)	180 (52.3)	353 (51.9)
Cohort 2	163 (48.5)	164 (47.7)	327 (48.1)
At least one FPM with dentine caries at 36 months			
Cohort 1	41 (50.0)	46 (63.0)	87 (56.1)
Cohort 2	41 (50.0)	27 (37.0)	68 (43.9)
Total			
Cohort 1	214 (51.2)	226 (54.2)	440 (52.7)
Cohort 2	204 (48.8)	191 (45.8)	395 (47.3)
No dentine caries in FPMs at 36 months			
Baseline caries			
Primary dentition free of caries into dentine	130 (38.7)	131 (38.1)	261 (38.4)
1–2 primary teeth with caries into dentine	68 (20.2)	69 (20.1)	137 (20.1)
≥ 3 primary teeth with caries into dentine	138 (41.1)	144 (41.9)	282 (41.5)
At least one FPM with dentine caries at 36 months			
Baseline caries			
Primary dentition free of caries into dentine	17 (20.7)	6 (8.2)	23 (14.8)
1–2 primary teeth with caries into dentine	8 (9.8)	11 (15.1)	19 (12.3)
≥ 3 primary teeth with caries into dentine	57 (69.5)	56 (76.7)	113 (72.9)
Total			
Baseline caries			
Primary dentition free of caries into dentine	147 (35.2)	137 (32.9)	284 (34.0)
1–2 primary teeth with caries into dentine	76 (18.2)	80 (19.2)	156 (18.7)
≥ 3 primary teeth with caries into dentine	195 (46.7)	200 (48.0)	395 (47.3)

Children in cohort 2 experienced less diseased teeth. Children in the FV arm with dentine caries on one or two primary teeth experienced more dentine caries in their FPMs than those in the FS arm. Those receiving FV who had more than three primary teeth with dentine caries were also marginally more likely to experience dentine caries in their FPMs than those receiving FS (48% vs. 46.7%).

The interaction between cohort and intervention arm is reported in *Table 17*. From this it is apparent that the interaction of arm and cohort is not statistically significant.

The interaction of baseline caries risk with trial arm does not quite reach conventional levels of statistical significance, as shown in *Table 18*. Those children treated with FV who had more caries at baseline in their primary dentition were more likely to develop caries at 36 months than those who received FS. However, caution should be used for the interpretation of these effects, as the subgroup sizes for baseline caries risk were small.

Secondary analysis for the primary outcome: proportion of children developing dentine caries (D_{4-6} MFT) on any first permanent molar at 36 months

To determine the impact of potential confounding factors, a covariate analysis of the primary outcome was undertaken from two perspectives: child level (*Table 19*) and school level (*Table 20*).

The numbers for the child-level covariate analyses were substantially lower than those for the primary outcome because of questionnaire non-responses. The only covariates that were significantly associated with outcome were frequency of tooth brushing (OR 0.36, 95% CI 0.21 to 0.60) and toothpaste type (OR 0.45, 95% CI 0.27 to 0.75). Those brushing twice or more a day were less likely to develop caries on their FPMs than those brushing once or less a day. Those using children's or other toothpaste were less likely to develop caries on their FPMs at 36 months. None of the covariates altered the main effect for arm.

Two further potential influencing factors on the primary outcome were examined: the size of the school, in terms of the number of children enrolled, and the socioeconomic level of the locality in which the school was situated, as determined by the WIMD.³⁶

TABLE 17 Subgroup analysis of the proportion of children with dentine caries (D_{4-6} MFT) on any FPM in the trial: differential intervention effect by cohort

	Adjusted ^a OR (95% CI)	p-value
FS	Reference	
FV	1.07 (0.66 to 1.74)	0.790
Baseline caries		
Primary dentition free of caries into dentine	Reference	
1–2 primary teeth with caries into dentine	1.62 (0.85 to 3.09)	0.140
≥ 3 primary teeth with caries into dentine	4.60 (2.84 to 7.44)	< 0.001
Sex		
Female	Reference	
Male	1.04 (0.73 to 1.50)	0.824
Cohort 1	Reference	
Cohort 2	1.19 (0.72 to 1.96)	0.500
	Reference	
Cohort 2 × FV arm	0.58 (0.28 to 1.21)	0.147

a FV compared with FS. Analysis adjusted for baseline caries prevalence and sex.

TABLE 18 Subgroup analysis of the proportion of children with ICDAS caries (levels 4–6) on any FPM in the trial: differential intervention effect by baseline caries risk group

	Adjusted ^a OR (95% CI)	p-value
FS	Reference	
FV	0.35 (0.13 to 0.92)	0.032
Baseline caries		
Primary dentition free of caries into dentine	Reference	
1–2 primary teeth with caries into dentine	0.90 (0.37 to 2.19)	0.811
≥ 3 primary teeth with caries into dentine	3.16 (1.75 to 5.72)	< 0.001
Sex		
Female	Reference	
Male	1.05 (0.73 to 1.50)	0.808
FV × 1–2 primary teeth with caries into dentine	3.89 (0.99 to 15.28)	0.051
FV × ≥ 3 primary teeth with caries into dentine	2.69 (0.93 to 7.72)	0.067

a FV compared with FS. Analysis adjusted for baseline caries prevalence and sex.

TABLE 19 The impact of child-level covariates between intervention arms on dentine caries (D₄₋₆MFT)

Covariate	Total N	FS or FV	Adjusted ^a OR (95% CI)	p-value
Global oral hygiene regimen	493	FS	Reference	
		FV	0.90 (0.55 to 1.45)	0.652
Additional fluoride	471	FS	Reference	
		FV	0.93 (0.57 to 1.50)	0.753
Cariogenic global score	487	FS	Reference	
		FV	0.85 (0.53 to 1.39)	0.526
Socioeconomic group	460	FS	Reference	
		FV	0.85 (0.51 to 1.41)	0.524
Frequency of tooth brushing	489	FS	Reference	
		FV	0.97 (0.59 to 1.59)	0.904
Toothpaste type	484	FS	Reference	
		FV	0.88 (0.54 to 1.44)	0.616
Length of time brushing tooth	467	FS	Reference	
		FV	0.99 (0.55 to 1.47)	0.666
WIMD child	834	FS	Reference	
		FV	0.85 (0.59 to 1.22)	0.371

a Adjusted for sex and baseline caries risk.

TABLE 20 The impact of school-level covariates between intervention arms on dentine caries (D₄₋₆MFT)

Covariate	n	FS or FV	Adjusted ^a OR (95% CI)	p-value	ICC
School size	835	FS	Reference	0.364	0.022
		FV	0.85 (0.59 to 1.22)		
WIMD school	835	FS	Reference	0.348	0.032
		FV	0.84 (0.58 to 1.21)		

^a Adjusted for sex and baseline caries risk.

When modelled using a two-level logistic model of child within school, neither school size nor the WIMD of the locality in which the school was located was significantly associated with the caries outcome at 36 months, and including them did not alter the main effect of intervention arm.

The effect of fissure sealant and fluoride varnish on caries prevention by tooth

The proportion of first permanent molar teeth caries-free at 36 months

The analyses reported above relate to the proportion of children developing new caries on any one of up to four treated FPMs, that is, a child-level outcome. The second main objective in this clinical trial was:

- the number of treated FPM teeth that were caries free at 36 months.

In both the FS and the FV arms of the trial, 120 FPM teeth (7.5% of all teeth) developed caries into dentine, required a restoration or were extracted (*Table 21*). A multilevel model (*Table 22*), adjusted for the number of decayed primary teeth at baseline and sex, confirmed that the difference between children receiving FS and children receiving FV was not statistically significant (OR 0.97, 95% CI 0.73 to 1.28; $p = 0.83$). A preliminary analysis showed that there was no significant differences between quadrants (upper right, upper left, lower right and lower left), but quadrant was retained in the model as a cluster level (ICC = 0.12).

This means that there was no difference in the proportion of FPM teeth developing decay into dentine between the arms of the trial.

A further analysis examined the severity of caries attack as determined by the number of teeth becoming carious per child. The proportion of children with dentine caries (D₄₋₆MFT) at 36 months by the number of FPMs by intervention arm is shown in *Table 23*. The proportion of FPMs per child developing dentine caries differed marginally between the intervention arms.

The significance of the difference between the intervention arms was tested using ordinal regression modelling (*Table 24*). Those children with three or four FPMs with caries into dentine were grouped together. A marginally smaller proportion of children who received FV developed caries into dentine in their FPMs at 36 months, although the difference from the FS arm was not statistically significant (OR 0.87, 95% CI 0.64 to 1.20).

'Threshold' represents the response variable in the ordered logistic regression.

TABLE 21 The proportion of FPM teeth with dentine caries (D₄₋₆MFT) at 36 months by intervention arm

	Intervention arm, n (%)		Total (N = 3205), n (%)
	FS (N = 1609)	FV (N = 1596)	
No caries	1489 (92.5)	1476 (92.5)	2965 (92.5)
Caries on FPM surface	120 (7.5)	120 (7.5)	240 (7.5)

TABLE 22 Multilevel model of quadrant within child for FPM caries at D₄₋₆MFT

	Unadjusted OR (95% CI)	p-value	Adjusted ^a OR (95% CI)	p-value
FS	Reference		Reference	
FV	1.03 (0.79 to 1.35)	0.825	0.97 (0.73 to 1.28)	0.830
Baseline caries				
Primary dentition free of caries into dentine			Reference	
1–2 primary teeth with caries into dentine			1.57 (0.90 to 2.74)	0.111
≥ 3 primary teeth with caries into dentine			5.66 (3.76 to 8.51)	< 0.001
Sex				
Female			Reference	
Male			1.00 (0.75 to 1.32)	0.972

^a Adjusted for sex and baseline caries risk.
ICC for quadrant = 0.120.

TABLE 23 The proportion of children developing dentine caries (D₄₋₆MFT) at 36 months by number of FPM by trial arm

	Intervention arm, n (%)		Total (N = 835), n (%)
	FS (N = 418)	FV (N = 417)	
No caries on any FPM	336 (80.4)	344 (82.5)	680 (81.4)
Caries on one FPM	53 (12.7)	43 (10.3)	96 (11.5)
Caries on two FPM	22 (5.3)	17 (4.1)	39 (4.7)
Caries on three FPM	5 (1.2)	9 (2.2)	14 (1.7)
Caries on four FPM	2 (0.5)	4 (1.0)	6 (0.7)

TABLE 24 Ordinal regression analysis of the number of FPMs with dentine caries, a restoration or extracted because of caries (D₄₋₆MFT) at 36 months by trial intervention arm

	Unadjusted OR (95% CI)	p-value	Adjusted ^a OR (95% CI)	p-value
FS	Reference		Reference	
FV	0.89 (0.65 to 1.22)	0.465	0.87 (0.64 to 1.20)	0.399
Threshold				
0 to 1			11.31 (7.16 to 17.86)	< 0.001
1 to 2			32.38 (19.60 to 55.51)	< 0.001
2 to 3			98.87 (53.37 to 183.14)	< 0.001
Baseline caries				
Primary dentition free of caries into dentine			Reference	
1–2 primary teeth with caries into dentine			1.54 (0.84 to 2.83)	0.167
≥ 3 primary teeth with caries into dentine			4.05 (2.59 to 6.35)	< 0.001
Sex				
Female			Reference	
Male			1.03 (0.75 to 1.41)	0.866

^a FV compared with FS. Analysis adjusted for baseline caries risk group, sex and number of FPMs in the trial.

The threshold estimates are the cut-off points that differentiate between ordered categories of the outcome. The OR for trial arm is not statistically significant (and no different from the logistic model), indicating no difference between the arms for the ordinal outcome of number of FPMs with caries per child.

The effect of fissure sealant and fluoride varnish by tooth surfaces

Because of its mode of action, FS can afford protection only to the occlusal tooth surface. By contrast, FV can afford protection to the occlusal and the mesial, buccal, lingual and distal (smooth) tooth surfaces. It was, therefore, important to determine if there was a difference between the intervention arms in the number of tooth surfaces affected.

Looking first at the proportion of tooth surfaces that developed caries into dentine or that were restored or extracted because of caries at 36 months (*Table 25*), the number of such surfaces affected was 169 (2.1%) in the FS arm and 181 (2.3%) in the FV arm.

Table 26 reports a multilevel model that examines the proportion of tooth surfaces affected by dentine caries (D₄₋₆MFS) within quadrant within child. There was no significant difference between the intervention arms in the number of FPM tooth surfaces developing caries (OR 1.06, 95% CI 0.84 to 1.33; $p = 0.619$).

TABLE 25 The number of surfaces with dentine caries, restored or that had been extracted (D₄₋₆MFS) at 36 months by intervention arm

Status	Intervention arm, n (%)		Total (N = 16,016), n (%)
	FS (N = 8041)	FV (N = 7975)	
Free of caries into dentine	7872 (97.9)	7794 (97.7)	15,666 (97.8)
D ₄₋₆ MFS	169 (2.1)	181 (2.3)	350 (2.2)

TABLE 26 Multilevel model of surfaces within quadrant within child for FPM dentine caries, restored or extracted tooth surfaces (D₄₋₆MFS)

	Unadjusted OR (95% CI)	p-value	Adjusted ^a OR (95% CI)	p-value
FS	Reference		Reference	
FV	1.17 (0.93 to 1.46)	0.177	1.06 (0.84 to 1.33)	0.619
Baseline caries				
Primary dentition free of caries into dentine			Reference	
1–2 primary teeth with caries into dentine			1.41 (0.86 to 2.33)	0.173
≥ 3 primary teeth with caries into dentine			6.50 (4.56 to 9.27)	< 0.001
Sex				
Female			Reference	
Male			1.38 (1.09 to 1.74)	0.007

^a FV compared with FS. Analysis adjusted for baseline caries prevalence and sex. ICC for quadrant = 0.197 and ICC for surface = 0.058.

Table 27 further reports on the severity of caries experience on the FPMs, as represented by the number of surfaces with caries into dentine as a proportion of the total number of surfaces affected. This shows the severity of caries experience within the trial arms.

Ordinal regression modelling was undertaken on the number of FPM surfaces per child developing caries. Those children with between 5 and 20 affected surfaces were combined into one group, owing to the small numbers in these categories. As shown in Table 28, there was no statistically significant difference between those receiving FS and those receiving FV, the model having been adjusted to account for the number of surfaces with caries per child (OR 0.87, 95% CI 0.64 to 1.19; $p = 0.385$), the number of decayed primary teeth at baseline and sex.

This means that there was no difference in the severity of the caries experience between the FS- and FV-treated children.

Caries experience on occlusal and non-occlusal surfaces

Although there was no difference between arms in the proportion or the total number of tooth surfaces affected by dentine caries, or in the severity of attack, it was necessary to check if there was a difference in treatment effect by type of surface. Table 29 shows the distribution of caries-affected occlusal and non-occlusal surfaces by trial arm. Although, overall, a significantly greater proportion of occlusal surfaces than smooth surfaces had developed caries into dentine at 36 months (6.4% vs. 1.1%), it is clear that the proportion of occlusal surfaces affected by dentine caries was remarkably similar in the FS and FV arms of the trial, at 6.5% and 6.3%, respectively. Minimal differences between the intervention arms in the proportion of smooth surfaces of FPMs developing caries were observed at 36 months (1.0% vs. 1.3%). A multilevel model that accounted for quadrant and surface-level clustering, adjusted to account for caries prevalence in the primary dentition at baseline, sex, surface type and surface by arm interactions, is reported in Table 30. As previously, children with three or more affected primary teeth at baseline were significantly more likely to develop dentine caries on a FPM by 36 months and, overall, there was a significant difference between the proportion of occlusal surfaces developing dentine caries and the proportion of non-occlusal surfaces developing dentine caries (OR 7.72, 95% CI 5.57 to 10.69). However, no significant difference was observed between the trial arms for the main effect or for the interaction of arm with surface type, indicating no differential effect of treatment on occlusal and non-occlusal surfaces.

TABLE 27 The number of FPM surfaces per participant developing dentine caries (D_{4-6} MFS) at 36 months by intervention arm

	Intervention arm, n (%)		Total ($N = 835$), n (%)
	FS ($N = 418$)	FV ($N = 417$)	
D_{4-6} MFS = 0	336 (80.4)	344 (82.5)	680 (81.4)
1 with caries	46 (11.0)	36 (8.6)	82 (9.8)
2 with caries	14 (3.3)	17 (4.1)	31 (3.7)
3 with caries	11 (2.6)	7 (1.7)	18 (2.2)
4 with caries	3 (0.7)	6 (1.4)	9 (1.1)
5 with caries	4 (1.0)	4 (1.0)	8 (1.0)
6 with caries	1 (0.2)	1 (0.2)	2 (0.2)
7 with caries	2 (0.5)	0	2 (0.2)
10 with caries	1 (0.2)	0	1 (0.1)
20 with caries	0	2 (0.5)	2 (0.2)

TABLE 28 Ordinal regression analysis of the number of FPM surfaces with dentine caries (D₄₋₆MFS) at 36 months by trial arm

	Unadjusted OR (95% CI)	p-value	Adjusted ^a OR (95% CI)	p-value
FS	Reference		Reference	
FV	0.89 (0.65 to 1.22)	0.456	0.87 (0.64 to 1.19)	0.385
Threshold 0 to 1			11.38 (7.20 to 17.98)	< 0.001
1 to 2			26.00 (15.93 to 42.42)	< 0.001
2 to 3			46.43 (27.37 to 78.75)	< 0.001
3 to 4			82.56 (45.76 to 148.94)	< 0.001
4 to 5			133.16 (63.37 to 259.34)	< 0.001
Baseline caries				
Primary dentition free of caries into dentine			Reference	
1–2 primary teeth with caries into dentine			1.54 (0.83 to 2.82)	0.166
≥ 3 primary teeth with caries into dentine			4.05 (2.58 to 6.34)	< 0.001
Sex				
Female			Reference	
Male			1.05 (0.76 to 1.43)	0.782

^a FV compared with FS. Analysis adjusted for baseline caries risk group, sex and number of FPMs in the trial.

TABLE 29 The proportion of dentine caries, restored or extracted (D₄₋₆MFS) at 36 months by occlusal and non-occlusal surfaces by intervention arm

Status	Intervention arm, n/N (%)		
	FS (N = 8041)	FV (N = 7975)	Total (N = 16,016)
Caries on non-occlusal surface	64/6432 (1.0)	81/6380 (1.3)	145/12,812 (1.1)
Caries on occlusal surface	105/1609 (6.5)	100/1595 (6.3)	205/3204 (6.4)

Complier average causal effect analysis

In a trial such as that reported here, compliance with the intended treatment regimen is an important consideration. Children participating in the trial were scheduled to be seen by the dental hygienist every 6 months, meaning a maximum of six times (at 0, 6, 12, 18, 24 and 30 months) during the course of the trial. The number of treatment visits attended by each child who also underwent a final clinical examination at 36 months is shown in *Table 31*. It is apparent that fidelity in this trial was excellent, with in excess of 70% of children attending all six treatment visits and 95% of children in the FS and FV arms of the trial attending at least five treatment visits. The association of treatment visits and final outcome by trial arm is shown in *Table 31*.

From *Table 31*, it is clear that there was little association between the number of treatment visits and the development of caries in either trial arm.

To determine the effects of adherence to the scheduled number of treatment visits, a CACE analysis was carried out (*Table 32*). As FS was the standard treatment in the Designed to Smile programme prior to the implementation of this trial, a CACE analysis was carried out, assuming FS as the 'control' with treatment visits set to a constant (zero) and FV as the active treatment. In this way it can be established if the number of FV treatment visits had any significant impact on the main treatment effect.

TABLE 30 Two-level multilevel model of surfaces within quadrant within child for FPM dentine caries (D₄₋₆MFT) including interaction with surface type

	Adjusted ^a OR (95% CI)	p-value
FS	Reference	
FV	1.25 (0.89 to 1.77)	0.202
Baseline caries		
Primary dentition free of caries into dentine	Reference	
1–2 primary teeth with caries into dentine	1.42 (0.86 to 2.36)	0.174
≥ 3 primary teeth with caries into dentine	6.96 (4.85 to 9.98)	< 0.001
Sex		
Female	Reference	
Male	1.38 (1.10 to 1.76)	0.007
Surface type		
Non-occlusal	Reference	
Occlusal	7.72 (5.57 to 10.69)	< 0.001
Surface by arm interaction		
(FV × occlusal surface)	0.75 (0.48 to 1.18)	0.217

^a FV compared with FS. Analysis adjusted for baseline caries prevalence and sex. ICC for quadrant = 0.213 and ICC for surface = 0.075.

TABLE 31 The association of treatment visits and the primary outcome (D₄₋₆MFT) on any FPM by intervention arm

Treatment visits	Intervention arm, n (%)			
	FS		FV	
	No FPM with D ₄₋₆ MFT (N = 336)	At least one FPM with D ₄₋₆ MFT (N = 82)	No FPM with D ₄₋₆ MFT (N = 344)	At least one FPM with D ₄₋₆ MFT (N = 73)
1	1 (0.3)	0 (0)	0	0
2	0	0	0	1 (1.4)
3	1 (0.3)	1 (1.4)	4 (1.2)	0
4	13 (3.9)	3 (3.7)	11 (3.2)	4 (5.5)
5	75 (22.3)	17 (20.7)	80 (23.3)	16 (21.9)
6	246 (73.2)	61 (74.4)	249 (72.4)	52 (71.2)

The coefficient for the number of treatment visits for FV was non-significant, indicating that increasing the number of visits does not have an impact on the proportion of children experiencing caries on their FPMs. The efficacy per visit was -0.005, indicating only a small decrease in the proportion of children with caries on any FPM for additional FV visits. This small effect is attributable to the high proportion of children attending at least five visits out of a maximum of six.

From this, it is concluded that adherence to the treatment protocol was not an influencing factor in the results obtained at 36 months.

TABLE 32 Complier average causal effect analysis

	Efficacy coefficient (95% CI)	p-value
Number of FV treatment visits	-0.005 (-0.014 to 0.004)	0.303
	OR (95% CI)	p-value
Baseline caries		
Primary dentition free of caries into dentine	Reference	
1–2 primary teeth with caries into dentine	1.37 (0.97 to 1.10)	0.310
≥ 3 primary teeth with caries into dentine	1.22 (1.16 to 1.30)	< 0.001
Sex		
Female	Reference	
Male	1.00 (0.95 to 1.05)	0.961

Adherence to the prespecified treatment window

The study protocol dictated that treatment visits should be scheduled within a 4-week window either side of the due 6-month treatment schedule. Adherence to this schedule is shown in *Table 33*. Overall, 71.6% of treatments were within the treatment window throughout the trial, and a further 26.1% were outside the schedule on only one occasion, a further indicator of the fidelity of the trial.

To test for the effect of adherence to the treatment window, a binary indicator was added to the primary model that categorised the participants as having received all of their treatment visits within the time window stated in the study protocol or having had at least one visit outside the treatment window. The likelihood of developing D₄₋₆MFT on any FPM was lower for those who received at least one treatment outside the study treatment window (OR 0.66, 0.43 to 1.00; $p = 0.052$). Although this effect was of borderline significance, the main effect of FS versus FV remained unchanged compared with the primary analysis (*Table 34*).

This demonstrates that any deviation from the scheduled treatment window did not impact on the overall results of the trial.

TABLE 33 The proportion of children with treatments outside the specified treatment window by intervention arm

Number of treatments outside window	Intervention arm, n (%)		Total (N = 835), n (%)
	FS (N = 418)	FV (N = 417)	
0	302 (72.2)	296 (71.0)	598 (71.6)
1	106 (25.4)	112 (26.9)	218 (26.1)
2	7 (1.7)	5 (1.2)	12 (1.4)
3	1 (0.2)	3 (0.7)	4 (0.5)
4	2 (0.5)	0	2 (0.2)
5	0	1 (0.2)	1 (0.1)

TABLE 34 The effect of treatment window on the development of D₄₋₆MFT on any FPM at 36 months

	Adjusted ^a OR (95% CI)	p-value
FS	Reference	
FV	0.84 (0.58 to 1.21)	0.341
Baseline caries		
Primary dentition free of caries into dentine	Reference	
1–2 primary teeth with caries into dentine	1.61 (0.84 to 3.06)	0.140
≥ 3 primary teeth with caries into dentine	4.61 (2.85 to 7.45)	< 0.001
Sex		
Female	Reference	
Male	1.05 (0.73 to 1.50)	0.811
All treatment within window	Reference	
At least one outside window	0.66 (0.43 to 1.00)	0.052

a Adjusted for sex and baseline caries risk group.

The effect of including enamel caries on trial outcome

The analysis reported in *Complier average causal effect analysis* at the D₄₋₆MFT level is in line with conventional reporting of dental clinical trials. In this study, dental caries was recorded using the ICDAS.²⁶ This index includes the recording of enamel caries. This section reports the effects of including enamel caries in the trial outcome data.

Table 35 shows the proportion of children developing enamel and dentine caries at the D₁₋₆MFT level at 36 months. The proportion of children who developed dental caries was higher in the FS arm (77.3%) than in the FV arm (67.6%). Adjusting for the number of decayed primary teeth at baseline and sex, a significant treatment effect between arms was apparent (Table 36). The OR for developing caries when enamel caries was included in the outcome measure was significant (OR 0.56, 95% CI 0.41 to 0.78), indicating a possible protective effect of FV for enamel caries lesions. This suggests that, although there was no difference between the trial arms in terms of caries into dentine prevented, the same does not hold true when enamel caries is included in the outcome measure. A significantly greater proportion of children did not develop either dentine or enamel caries on any FPM included in the trial when treated with FV (32.4% vs. 22.7%).

The consequences of including enamel caries were further explored to examine the effect by occlusal versus non-occlusal surfaces. In the FS arm of the trial, 6.7% of non-occlusal surfaces developed caries at the D₁₋₆MFS level, compared with 5.6% in the FV arm. On occlusal surfaces, the figures for the development of either enamel or dentine caries were 39.2% and 40.5% in the case of FS and FV, respectively (Table 37).

TABLE 35 The proportion of children with (D₁₋₆MFT) on any FPM in the trial, at 36 months by trial arm

	Intervention arm, n (%)		Total (N = 835), n (%)
	FS (N = 418)	FV (N = 417)	
No caries on any FPM	95 (22.7)	135 (32.4)	230 (27.5)
Caries at D ₁₋₆ MFT level on at least one FPM	323 (77.3)	282 (67.6)	605 (72.5)

TABLE 36 The proportion of children with (D₁₋₆MFT) on any FPM in the trial by intervention arm at 36 months

	Unadjusted OR (95% CI)	p-value	Adjusted ^a OR (95% CI)	p-value
FS	Reference		Reference	
FV	0.61 (0.45 to 0.84)	0.002	0.56 (0.41 to 0.78)	0.001
Baseline caries				
Primary dentition free of caries into dentine			Reference	
1–2 primary teeth with caries into dentine			2.37 (1.54 to 3.64)	< 0.001
≥ 3 primary teeth with caries into dentine			5.12 (3.54 to 7.40)	< 0.001
Sex				
Female			Reference	
Male			0.81 (0.58 to 1.11)	0.187

a FV compared with FS. Analysis adjusted for number of decayed primary teeth at baseline and sex.

TABLE 37 The proportion of caries experience D₁₋₆MFS at 36 months by occlusal and non-occlusal surfaces by intervention arm

	Intervention arm, n/N (%)		Total (N = 16,016), n/N (%)
	FS (N = 8041)	FV (N = 7975)	
Caries on non-occlusal surface	429/6432 (6.7)	360/6380 (5.6)	789/12812 (6.2)
Caries on occlusal surface	631/1609 (39.2)	646/1595 (40.5)	1277/3204 (39.9)

A multilevel model confirmed a statistically significant difference in favour of the FV-treated surfaces. The clinical significance of this finding is unclear. It possibly shows FV to be protective for early-phase caries compared with FS (Table 38). However, this does not translate into a protective effect for dentine caries compared with FS.

To further explore the effect of including enamel caries, analyses were conducted for enamel and dentine caries at the D₂₋₆MFT and D₃₋₆MFT levels. Using both of these caries levels as the cut-off point for determining the clinical outcome, children in the FV arm were significantly less likely to develop caries experience on at least one FPM than those in the FS group: D₂₋₆MFT (OR 0.65, 95% CI 0.49 to 0.88) and D₃₋₆MFT (OR 0.66, 95% CI 0.48 to 0.90).

Whole-mouth caries experience at 36 months

Although the caries-preventative effect of FS is limited to the occlusal surface of the treated tooth, it is possible that, by elevating the general intraoral fluoride concentration, there may be a 'wash-over' effect as a result of applying FV to the FPMs. To examine this possible difference between the treatments, the caries increment on all permanent teeth present at the 36-month assessment was examined.

Table 39 shows the proportion of children with caries (D₄₋₆MFT) on any permanent tooth at 36 months.

To examine the difference in the number of affected teeth, Poisson and binomial distribution modelling were carried out. Furthermore, to account for the excess of non-affected individuals, zero inflated models were conducted to improve model fit. The results are shown in Table 40. No significant differences were observed between intervention arms. This means that no wash-over effect was observed. A similar analysis was carried out on the D₄₋₆MFS scores. No significant difference was observed between FS- and FV-treated children.

TABLE 38 Multilevel model of surfaces within quadrant within child caries experience D₁₋₆MFS at 36 months including interaction with surface type

	Adjusted ^a OR (95% CI)	p-value
FS	Reference	
FV	0.80 (0.68 to 0.93)	0.004
Baseline caries		
Primary dentition free of caries into dentine	Reference	
1–2 primary teeth with caries into dentine	2.00 (1.69 to 2.36)	< 0.001
≥ 3 primary teeth with caries into dentine	4.37 (3.82 to 4.99)	< 0.001
Sex		
Female	Reference	
Male	0.92 (0.83 to 1.03)	0.148
Surface type		
Non-occlusal	Reference	
Occlusal	19.44 (5.78 to 65.43)	< 0.001
Surface by arm interaction		
(Varnish × occlusal surface)	1.29 (1.04 to 1.60)	0.019

^a FV compared with FS. Analysis adjusted for baseline caries prevalence and sex. ICC for quadrant = 0 and ICC for surface = 0.268.

TABLE 39 The total number of permanent teeth affected by D₄₋₆MFT by intervention arm

Number of permanent teeth with D ₄₋₆ MFT	Intervention arm, n (%)	
	FS (N = 418)	FV (N = 417)
0	326 (78.0)	334 (80.1)
1	56 (13.4)	42 (10.1)
2	27 (6.5)	26 (6.2)
3	5 (1.2)	11 (2.6)
4	3 (0.7)	4 (1.0)
6	1 (0.2)	0

TABLE 40 Analysis of the impact of FS and FV on all permanent teeth at 36 months

	Adjusted ^a incidence rate ratio (95% CI)	p-value	Akaike information criterion
Poisson	0.94 (0.74 to 1.20)	0.624	1171
Negative binomial	0.93 (0.82 to 1.46)	0.549	1104
Zero inflated Poisson	1.01 (0.76 to 1.35)	0.920	1091
Zero inflated negative binomial	1.01 (0.75 to 1.35)	0.924	1093

^a FV compared with FS. Analysis adjusted for baseline caries prevalence and sex.

The effect of trial interventions at 12 and 24 months

All of the analyses reported above relate to the clinical outcome at 36 months, the a priori time period agreed for the determination of the primary clinical outcome. Although no significant difference was observed between FS and FV at 36 months, the question arises as to whether the outcome would have been different had the trial terminated at 12 or 24 months.

At the 12-month examination, 36 (8%) children who had received FS experienced dental decay in at least one FPM at the D₄₋₆MFT level, compared with 37 (8.3%) of those treated with FV. By 24 months, the numbers similarly affected had increased to 61 (13.9%) and 63 (14.9%) in the FS and FV arms of the trial, respectively (Table 41).

A repeated measures analysis was carried out using the proportion of children experiencing caries D₄₋₆MFT on any FPM at 12, 24 and 36 months. Although the proportion of children experiencing caries was significantly higher at 24 months than at 12 months and at 36 months than at 12 months, there were no significant differential effects of treatment by time, and the interaction effect was dropped from the model (Table 42).

It can, therefore, be concluded that there was no statistically significant difference between the treatments under investigation at any of the annual examinations.

Sealant retention

The effectiveness of FS is influenced by retention,⁴⁰ and complete sealants are known to be more effective than partial sealants.⁴¹

TABLE 41 The proportion of children with caries (D₄₋₆MFT) on any treated FPM in the trial at each annual examination by intervention arm

	Time point (months), n (%)					
	12		24		36	
	FS (N = 450)	FV (N = 444)	FS (N = 439)	FV (N = 424)	FS (N = 418)	FV (N = 417)
No caries on any FPM	414 (92.0)	407 (91.7)	378 (86.1)	361 (85.1)	336 (80.4)	344 (82.5)
Caries on at least one FPM	36 (8.0)	37 (8.3)	61 (13.9)	63 (14.9)	82 (19.6)	73 (17.5)

TABLE 42 A repeated measures logistic regression of the proportion of children with caries (D₄₋₆MFT) on any treated FPM

	Treatment effect (sealant is reference)		Examination (time point, months) (12 months is reference)			
			24		36	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Proportion with caries at ICDAS 4–6	0.96 (0.76 to 1.21)	0.878	1.92 (1.41 to 2.62)	< 0.001	2.64 (1.95 to 3.56)	< 0.001

Model is adjusted for sex and baseline caries risk.

In this trial, children were examined at 6-month intervals and any deficient sealants were repaired. Policy was to seal teeth as soon as sufficient tooth surface had erupted, so, particularly in the case of upper molars, teeth were on occasion sealed over two visits as the tooth erupted. The status of the sealants as recorded by the dental hygienists is shown in *Table 43*.

TABLE 43 Sealant status at each treatment visit

	Time point (months), <i>n</i> (%)				
	6	12	18	24	30
UR intact	198 (44.7)	269 (68.3)	298 (76.4)	300 (76.7)	275 (74.5)
Partial	111 (25.1)	70 (17.8)	72 (18.5)	78 (19.9)	86 (23.3)
Lost	2 (0.5)	5 (1.3)	2 (0.5)	7 (1.8)	2 (0.5)
Tooth unerupted	40 (9.0)	7 (1.8)	3 (0.8)	2 (0.5)	1 (0.3)
Tooth extracted	0	0	0	0	0
Tooth previously unerupted	92 (20.8)	43 (10.9)	16 (4.1)	4 (1.0)	5 (1.4)
<i>N</i>	443	394	391	391	369
Missing		9	6		1
UL intact	172 (40.2)	259 (64.3)	298 (74.5)	285 (72.5)	275 (73.7)
Partial	130 (30.4)	90 (22.3)	82 (20.5)	93 (23.7)	84 (22.5)
Lost	4 (0.9)	10 (2.5)	5 (1.2)	10 (2.5)	9 (2.4)
Tooth unerupted	22 (5.1)	6 (1.5)	0	1 (0.3)	1 (0.3)
Tooth extracted	0	0	0	0	1 (0.3)
Tooth previously unerupted	100 (23.4)	38 (9.4)	15 (3.8)	4 (1.0)	3 (0.8)
<i>N</i>	428	403	398	393	373
Missing	2	7	5	2	2
LR intact	274 (62.3)	311 (78.1)	339 (85.8)	350 (88.4)	324 (88.0)
Partial	33 (7.5)	22 (5.5)	23 (5.8)	20 (5.1)	32 (8.7)
Lost	1 (0.2)	1 (0.3)	2 (0.5)	5 (1.3)	2 (0.5)
Tooth unerupted	41 (9.3)	16 (4.0)	10 (2.5)	3 (0.8)	2 (0.5)
Tooth extracted	0	0	0	0	0
Tooth previously unerupted	91 (20.7)	48 (12.1)	21 (5.3)	18 (4.5)	8 (2.2)
<i>N</i>	440	398	395	396	368
Missing		6	7	1	3
LL intact	262 (59.4)	314 (78.1)	346 (87.2)	347 (87.8)	340 (91.4)
Partial	30 (6.8)	24 (6.0)	17 (4.3)	28 (7.1)	19 (5.1)
Lost	4 (0.9)	2 (0.5)	2 (0.5)	4 (1.0)	3 (0.8)
Tooth unerupted	32 (7.3)	16 (4.0)	9 (2.3)	5 (1.3)	2 (0.5)
Tooth extracted	0	0	0	0	0
Tooth previously unerupted	113 (25.6)	46 (11.4)	23 (5.8)	11 (2.8)	8 (2.2)
<i>N</i>	441	402	397	395	372
Missing		8	8	4	2

LL, lower left; LR, lower right; UL, upper left; UR, upper right.

Examiner reproducibility

The kappa statistics for agreement with the gold standard examiner are shown in *Table 44*. Based on Landis and Koch,⁴² all of the examiners show substantial agreement (0.69–0.8) or excellent agreement (0.81–1) throughout the study. Calibration was at the $d/D_{0-3}:d/D_{4-6}$ level.

To determine intra-examiner reproducibility, 5% of participants were re-examined. The resultant kappa values (DMFT sound surfaces excluded) are shown in *Table 45*.

Treatment time

The time taken to provide the FS and FV treatments, recorded as time spent in the dental chair by each child at the baseline and 30-month examinations, is recorded in *Table 46*.

At baseline, the mean treatment time was higher for the FS arm than for the FV arm, whereas at 30 months the mean treatment time was slightly lower for the FS arm. This is because, as the trial progressed, fewer FSs needed to be placed in the FS arm, although some time was needed to repair FS when deficient. At baseline, 1301 FSs were placed, whereas at 12 months only 313 top-up treatments were performed. By 24 months, the number of top-up treatments had dropped to 178, and this dropped further to 130 at the 30-month time point, which was the final treatment.

Data were transformed using a natural log for regression analyses and, hence, effects are interpreted as percentage difference between arms.

TABLE 44 Calibration (inter-examiner reproducibility)

Assessment	Examiner					
	1	2	3	4	5	6
2011	0.754	0.819	0.749			
2012	0.830	0.883	0.914			
2013	0.754	0.915		0.768		
2014	0.938				0.801	0.690
2015	0.931					0.740

TABLE 45 Intra-examiner reproducibility

Assessment	Examiner					
	1	2	3	4	5	6
2011	0.929	0.908	0.818			
2012	0.939	0.928	0.657			
2013	0.925	0.946		0.909		
2014	0.8500				0.960	0.830
2015						0.972

TABLE 46 Mean treatment time (seconds) for FS and FV at baseline and 30 months

	Intervention arm				Overall	
	FS		FV			
	<i>n</i>	Mean (SD)	<i>n</i>	Mean (SD)	<i>n</i>	Mean (SD)
Baseline	467	533.0 (189.90)	463	190.5 (57.68)	930	362.5 (221.58)
30 months	424	130.0 (119.75)	418	151.1 (46.38)	842	140.5 (91.60)

SD, standard deviation.

At both time points, the addition of school as a level in a two-level regression (model 1) does not change the effect compared with the single-level model (model 2). At baseline, times were significantly lower in the FV arm, but at 30 months the difference was in the opposite direction (*Table 47*). These findings are in line with clinical expectations. At baseline, it takes much longer to place the FS because of the more involved clinical nature of the procedure, compared with the less complex method of FV placement.

Adverse effects

Throughout the trial adverse effects either during treatment or in the period thereafter were recorded as described in *Chapter 2*. For the entire duration of the trial, no adverse effects were reported.

Summary

This chapter has reported the clinical findings of the trial. The main findings are as follows.

- Children were recruited to the trial in two cohorts over successive school years and followed for 36 months. Of the 514 and 502 children randomised to the FS and FV treatments, respectively, 418 and 417 remained at 36 months [more than the 313 required per trial arm, as detailed in the power calculation (see *Chapter 2*)]. The majority of those not completing the trial moved to a non-participating school.
- There were no significant differences in participant characteristics between trial arms at baseline in those randomised, those who withdrew or were lost to follow-up and in those who completed the trial.
- The OR of developing caries in the FV arm compared with the FS arm was 0.87 (95% CI 0.61 to 1.23) in the unadjusted model, that is, the proportion of children who received FV who were likely to develop caries into dentine was lower than the proportion of those developing dentine caries in the FS arm, but this difference was not statistically significant. As sex and baseline caries risk group were used to balance the randomisation, an adjusted model was also performed and was taken as the primary analysis. The OR for developing caries in the FV arm was 0.84 (95% CI 0.59 to 1.21) in the adjusted model.

TABLE 47 Linear regression of treatment time at baseline and 30 months

	Effect (percentage difference) (95% CI)	<i>p</i> -value	ICC
Baseline, model 1	0.37 (0.36 to 0.39)	< 0.001	0.142
Baseline, model 2	0.37 (0.35 to 0.39)	< 0.001	n/a
30 months, model 1	1.66 (1.52 to 1.80)	< 0.001	0.117
30 months, model 2	1.64 (1.50 to 1.79)	< 0.001	n/a

n/a, not applicable.

- Adjusting for baseline caries experience in the primary dentition, school attended (size and deprivation score) did not affect the primary outcome of the trial.
- None of the covariates examined (fluoride use, oral hygiene regime, diet or deprivation) made any difference to the primary outcome of no significant difference between trial arms.
- A subsequent analysis examining differences between intervention arms at tooth level did not show any difference in the number of teeth developing decay into dentine between the arms of the trial.
- Examining the outcome at tooth-surface level showed that, although a significantly greater proportion of caries experience occurred on occlusal surfaces, there were no significant differences by trial arm.
- Fidelity in the trial was excellent, with 95% of the children receiving treatment at five or six of the six scheduled treatment sessions over the 36 months. Overall, 71.6% of treatments were within the treatment window throughout the trial, and a further 26.1% were outside the schedule on only one occasion.
- As per the trial protocol, and in line with convention, decay into dentine, as a cavity, restoration or tooth extracted because of caries, was taken as the caries level for the primary reported outcome. As the ICDAS was used to record caries, the effect of including enamel caries in the analysis was also determined. This resulted in the only analysis to suggest a significant difference between trial arms. The percentage of children in the FV arm of the study who developed decay at the D₁₋₆MFT level was 67.6%, compared with 77.3% of FS-treated children (adjusted OR 0.56, 95% CI 0.41 to 0.78).
- There was no evidence of any 'wash-over' effect on caries prevention in those treated with FV.
- There were no significant differences in caries outcome between trial intervention arms at the 12- or 24-month time points.

Chapter 4 reports on the economic aspects of the trial.

Chapter 4 Health economic evaluation: methods and results

Introduction

The recently updated Cochrane review¹⁶ highlighted the scarcity and clinical diversity of data, making it difficult to draw clear conclusions on the effectiveness of FS versus FV in preventing dental caries. This review did not undertake a review of the relative cost-effectiveness of these two technologies and neither could any comparable economic evaluations be found in a rapid review of the health economics literature conducted as part of the health economic analysis plan. This chapter reports on the methods and results of the economic evaluation conducted alongside the trial. The objectives were to establish the:

- costs and budget impact of FS and FV delivered in a community/school setting
- relative cost-effectiveness of these technologies.

Health economic methods for the within-trial analysis

Assessment of costs

Costs were considered from the perspective of the NHS (i.e. direct health-care costs associated with the interventions) and from a partial societal perspective that considered the costs to the family and school (education sector).

The intervention costs were obtained from discussion with the trial team and MDC staff and from data collected as part of the trial case report forms. Research costs (such as the costs of the calibration training or costs of storing the technologies to be compliant with MHRA guidelines) were not included. With the technologies for both interventions being delivered in an established MDC, the costs of the clinic in the base case (e.g. costs of the van, running costs or equipment costs) were not included, as these are equivalent. However, to illustrate the costs associated with the delivery of the technologies within a MDC setting, we reported a separate cost with the MDC included.

The main intervention costs were (1) acquisition costs for FS and FV and (2) costs associated with the delivery of the technologies (including the clinical assessments). The costs of the FS and FV were taken from the trial protocol, that is, it was assumed that a standard dosage was applied to all trial participants and, when required, the costs of any reapplication were also calculated when they were recorded. The costs of delivery were calculated from 'time in chair' information contained within the case report form for each participant visit. The skill mix and grade of staff involved in the visit were obtained from the clinical staff providing the interventions. In addition, any specific materials or equipment used in the application of the FS or FV were obtained from the clinical staff. These costs were aggregated and an average intervention cost per participant in each trial arm was calculated (*Table 48*).

Information about the other health-care visits associated with dental-related problems for each trial participant was obtained from a parent resource utilisation questionnaire (the DHQ; see *Appendix 13*). This captured information on dental health-care visits (e.g. to the family dentist), other health-care contacts (e.g. general practitioner or hospital) as a result of dental health problems and any prescriptions (e.g. painkillers or antibiotics) for dental health problems. As it would have been implausible to ask the parent/carer precise information about which tooth was affected, information was collected from the parent/carer on all dental health visits and events related to his or her child. The DHQ was completed by the main parent/carer at baseline and at 12, 24 and 36 months.

TABLE 48 Summary of intervention resource, unit costs and source

Basis of estimate	Unit cost (£)	Per hour (£)	Data sources
Dentistry staff band 3 × 1	–	9.20	NHS Staff Agenda for Change ⁴³
Dentistry staff band 4 × 1	–	10.58	NHS Staff Agenda for Change ⁴³
Dentistry staff band 5 × 0.65	–	12.62	NHS Staff Agenda for Change ⁴³
Administration staff (band 3) × 1	–	9.20	NHS Staff Agenda for Change ⁴³
Administration staff (band 4) × 1	–	10.58	NHS Staff Agenda for Change ⁴³
FV (Duraphat)	2.00	–	Dental supplier ^a
Sealant (Delton)	2.50	–	Dental supplier ^a
Clinical disposables (e.g. gloves, cotton wool, bib, etc.)	2.50	–	Dental supplier ^a
Sterilisation costs	1.75	–	Cardiff and Vale UHB ^b

a www.henryschein.co.uk (accessed in March 2016).

b www.cardiffandvaleuhb.wales.nhs.uk/home (accessed in March 2016).

Additional costs incurred by the family were also captured in the DHQ. This included any travel time and time off work/other activities associated with a health-care contact. The cost of caring for the child was also considered as a result of a dental health problem (e.g. day off work to care for the child). The main parent/carer was asked to estimate the time the child had off school as a result of a dental health problem.

Cost associated with travel time (using published government mileage rates) and time off work to attend health-care appointments with the child or the time taken to care for a child off school was calculated using a human capital approach. The value of work as well as leisure time was estimated by applying hourly rates, according to the parents' professions, to the time expended because of dental health problems during the trial period. Hourly rates of household/domestic help were used to cost the time of unemployed parents.

To capture the costs to the school, a series of questions were given to the head teacher as part of the process evaluation. These questions asked the head teacher to estimate the time the child had away from school activities in order to receive the interventions, any time required by the teacher or other support staff (e.g. to settle a child back into the classroom) and any other costs incurred by the school to support (e.g. administration time).

Prior to commencement of the trial, the DHQ, alongside the CHU-9D, was piloted for comprehensiveness, ease of completion, recall and accuracy in a primary school in South Wales, which was not included in the trial, with a similar sociodemographic to the trial population. A protocol was developed (available from the chapter author on request), with ethics approval given by Swansea University School of Human and Health Sciences prior to the pilot evaluation. Of 30 children who were given a pack to take home, six responses were obtained (20% response rate). All parents completed a postal questionnaire, with all responses indicating that their child had no difficulties understanding or completing the CHU-9D. In addition, the PPI representative on the TSC reviewed both questionnaires to check for readability and comprehension.

When possible, unit costs for the UK were applied [e.g. Personal and Social Services Research Unit,⁴⁴ *British National Formulary* (BNF),⁴⁵ NHS reference costs⁴⁶] to increase generalisability. However, to ensure that the skill mix of the MDC was fully considered in the analysis, local salary scales from NHS Wales⁴⁷ were obtained, and these were fully agreed with the trial team prior to analysis. These are reported in *Table 48*.

A summary of the other resource items, unit costs and sources is given in *Table 49*.

TABLE 49 Summary of other resource items, unit costs and sources

Health service resource utilisation	Unit cost (£)	Source
Dentist	110	Average weighted NHS Reference Cost 2014/15, ⁴⁶ M01a-3b
Socioeconomic classification wages per hour	Various	Office for National Statistics, 2015 ⁴⁸
Cost to schools attributed to absence	Various	GOV.uk ^a
Medicines	Various	BNF, 2015 ⁴⁵

a www.gov.uk/school-attendance-absence/overview (accessed on 1 June 2015).

The intervention costs and health-care utilisation costs were summated to give the total cost per participant for each arm (NHS costs), with the wider costs to the family and school reported separately (see *Table 54*).

Valuation of costs

All data were valued in monetary terms (£), and the price year of 2015 was applied to costs (representing the end point of the trial). As follow-up was beyond 12 months, discounting of 3.5% was applied, in line with the National Institute for Health and Care Excellence (NICE) reference case for health technologies⁵⁷ for the base-case costs. All costs were summarised into the different cost categories, with means and standard deviations (SDs) produced. A total cost (means and 95% CIs) was calculated for each trial arm, with differences reported using a Levene's test for equality *t*-test and with statistical significance accepted at the 5% level. When missing data existed, a simple weighted average cost based on known cost histories based on accepted methods was used.⁴⁹

To take into account the possible impact of skewness in cost data, the distribution of costs for normality were examined, as was the impact of removing extreme outliers from the analysis. When required, the sensitivity of the results was checked by considering appropriate transformation.⁵⁰

Outcomes used in the health economic analysis

Caries avoided

The data from the main trial were used to calculate the percentage of dentine caries (D₄₋₆MFT) avoided at 36 months.

Quality-adjusted life-years using the Child Health Utility Index 9D

The CHU-9D is a child-specific generic preference-based measure of HRQoL. It consists of a descriptive system of nine questions and a set of preference weights based on five levels with a recall period of today/last night. The CHU-9D allows the generation of utility values for each health state to enable the calculation of QALYs.^{51,52}

The CHU-9D was originally intended for use in a population aged 7–11 years. Prior to commencement of the trial, the original developer (Dr Katherine Stevens) was contacted to discuss whether or not it could be used in a younger age group, and there were no major concerns with regard to the trial's slightly younger age group. The trial team were mindful of the trial population and the potential variance in ability to self-complete the CHU-9D. The CHU-9D was piloted in a non-participating school in South Wales, with a debriefing interview completed by the parent/carer to assess any problems in its use. No issues were identified. Since the commencement of the trial, further studies have reported the use of the CHU-9D in a comparable age group to the trial population at study entry.^{53,54}

The CHU-9D was delivered to the child's home address with instructions given to complete at 12, 24 and 36 months. The instruction given was that either the child should self-complete or that the parent/carer would read the questions aloud to the child who would give his or her response. Owing to the practicalities of the trial, it was deemed unfeasible to collect the CHU-9D from the child, for example in school. Thus, the administration of the CHU-9D in this context may have resulted in under-/over-estimation of QoL, as it was not possible to verify whether or not this had been reported by the child himself/herself. However, this is expected to be similar across both study arms. The CHU-9D scores were computed for each time point and the QALY was calculated to obtain the difference in QALYs between the two trial arms at 36 months. In accordance with good practice, appropriate methods were explored to take into account missing data on the CHU-9D and subsequent QALY calculation.

Quality-adjusted tooth-year

Published utilities and clinical data used to derive the tooth-year were derived in order to generate a QATY. A QATY will estimate the production of additional years of life (tooth-year) of each tooth adjusted for the quality of that tooth. An unrestored tooth has a QATY of 1 in the year it was restoration free, although a restored, crowned or root canal-treated tooth has a QATY of less than perfect (i.e. less than 1) in the year that it was restored and in subsequent years. The QATY for an extracted tooth is equal to 0 in that year and subsequent years.

Although the QATY is seen as potentially useful in providing a more dental-specific analogy to the QALY, it has had limited use within the literature because of the limitations of being compared across different interventions and the lack of robust methodological work in deriving suitable utilities in order to populate the 'Q' element of the QATY. Owing to the lack of resources to undertake necessary methodological work to derive precise estimates of dental-specific utilities in children, this was intended to be an exploratory analysis only. Thus, only a one-way sensitivity analysis was undertaken.

The trial data were used to provide a series of health states associated with the tooth state of the four index teeth in the trial, based on the caries status. Published utilities were assigned from the published utilities from the Fyffe and Kay⁵⁵ study and from an economic analysis on the cost-effectiveness of oral health programmes⁵⁶ and were agreed with the trial team (*Table 50*).

A combined 'FPM utility' from the scores using the mean of the four tooth state utilities is as follows:

$$\sum_{i=1}^4 \frac{U_i}{n}. \quad (1)$$

TABLE 50 Quality-adjusted tooth-year tooth utility reasoning

State	Utility	Comments
Sound tooth or sound and sealed tooth (completely caries free)	1	As per Fyffe and Kay ⁵⁵
Unruptured tooth	1	As per Fyffe and Kay ⁵⁵
Tooth with enamel caries (D ₁₋₃) either sealed or unsealed	0.95	A tooth in this condition can be 'healed' or the lesion stopped from progressing, so although in the early disease stages and not as desirable as a totally sound tooth, this state is more desirable than a filled tooth. Fyffe and Kay have no utility for this state
Filled tooth (FT)	0.90	As per Fyffe and Kay ⁵⁵
Tooth with dentine caries (D ₄₋₆)	0.81	D ₄₋₆ is the equivalent to Fyffe and Kay's ⁵⁵ decayed and non-painful posterior tooth
Extracted tooth	0	As per Fyffe and Kay ⁵⁵

Analysis

Within-trial analysis

A series of incremental cost-effectiveness analyses were planned: (1) an incremental cost per caries avoided at 36 months and (2) an incremental cost per QALY (cost-utility). As part of a secondary analysis, costs and QALYs were examined. If one technology was both more effective and less costly, it would be considered to dominate the other technology and, as such, an ICER would not be reported. When there was no such dominance, an ICER would be calculated.

Univariate sensitivity analyses for all ICERs were recalculated after changing the value of a range of parameters individually to examine the uncertainty around the ICER (Table 51).

A probabilistic sensitivity analysis undertaken for the cost-utility analysis (CUA), with changes to the values of all chosen parameters (usually within the 95% CI or a reasonable, defined range), calculated the probability that the intervention was cost-effective in accordance with commonly accepted norms (£20,000–30,000 per incremental QALY gained).⁵⁷ Uncertainty associated with the individual parameters was considered.

Bootstrapping was used to construct data sets of the same trial population size by sampling at random with replacement over 1000 times. Cost-effectiveness acceptability curves (CEACs) were produced.

TABLE 51 Parameters assessed in the univariate sensitivity analysis

Parameter	Intervention arm (£)						Analysis	Justification/source
	FS			FV				
	Base case	Lower range	Upper range	Base case	Lower range	Upper range		
Costs (£)								
Staff costs of delivering the technology	74.12	51.88	96.36	64.16	44.91	83.41	BI	± 30% from trial data
One-off application of FS	14.24	9.97	18.51	–	–	–	BI	± 30% from trial data
FV application in school by dental hygienist	–	–	–	11.48	8.04	14.92	BI	± 30% from trial data
Delivery within school with MDC	95.73	67.01	124.45	86.33	60.43	112.23	BI	± 30% from trial data
Health-care resource usage for dental health problems (95% CI)	–68.13 (–5.63 to –130.63)						ICER	Based on 95% CIs from trial data
Clinical effects								
Caries avoided (95% CI)	0.021 (–0.0317 to 0.0738)						ICER	Based on 95% CIs from trial data
Health outcomes								
Changes in QALY estimates (95% CI)	0.002 (–0.010 to 0.005)						ICER	Based on 95% CIs from trial data
Changes in QALY estimates (95% CI)	0.007 (–0.068 to 0.011)						ICER	Based on 95% CIs from trial data
BI, budget impact.								

Budget impact analysis

A budget impact analysis to compare the costs to the NHS of FS versus FV was undertaken using the estimations of costs of the two interventions derived from the trial. The total budget impact for all patients within the trial population was calculated and examined the potential cost saving on a per-patient basis based on being treated with FS versus FV within the current intervention mix (based on the MDC). The impact to NHS budgets was estimated at 3 years. No discounting was applied to the budget impact analysis.

Model-based analysis

Deterministic sensitivity analyses were conducted to estimate the worst- and best-case scenarios of the budget impact of FS versus FV by using the lower and upper costs derived from the trial. The different scenarios that could impact on NHS budgets were (1) the cost of the intervention using a best-case/worst-case scenario; (2) the inclusion of the costs of the MDC; (3) the delivery of FV by a community dental nurse in a 'classroom' setting (i.e. not requiring a MDC but reflecting the potential for this technology to be delivered in a single application with minimal equipment/resources); and (4) the application of FV by a dental hygienist alone within a classroom/school medical room setting).

To assess the longer-term cost-effectiveness of FS versus FV in preventing dental caries in children, post-trial modelling was undertaken. As no suitable model could be identified from the literature search for adaptation, a de novo decision-analytic model was constructed. A UK NHS and Personal Social Services perspective was adopted in the analysis, in line with NICE methodological recommendations.⁵⁷ In the base case, costs and benefits were discounted at a rate of 3.5%.

Model structure

A Markov cohort simulation model, written in Microsoft Excel® 2013, version 15 (Microsoft Corporation, Redmond, WA, USA), was developed, with a 3-month time cycle employed in order to reflect an appropriate time point for caries progression to occur. Half-cycle corrections were applied. The time horizon of 5 and 10 years was chosen as sufficient to reflect potential changes in the change of progression of dental caries as a result of FS and FV in children up until the onset of adulthood. Although a lifetime horizon was considered, the lack of suitable evidence to make plausible assumptions about the longer-term effects of FS and FV resulted in an amendment to the original protocol plan. This was agreed with the trial team.

For FS and FV utilisation, Markov modelling allows for the construction of an arbitrary complex chain of events that represents the natural history of sealant retention, caries formation and their associated health states.⁵⁸ A sealed tooth may lose its seal and remain sound, may be resealed or may transition to caries. Caries may be restored. A restored tooth may develop further caries and this may finally lead to the tooth being lost. Varnished teeth represented the second intervention arm. A varnished tooth may develop caries, after which the pathway is the same as that for a tooth that develops caries after losing its seal. A lost/removed tooth was the absorbing state in the model.

A model structure was developed outlining the disease pathways and validated with the trial team before the model was built in Microsoft Excel. An outline of the model structure is given in *Figure 6*.

Key model assumptions

The model assumed that the population was the same as the trial population in terms of baseline characteristics at entry into the model. Children would be eligible to receive FS and FV as specified in the trial. After trial completion, children would no longer be in the Designed to Smile programme (i.e. they would have entered secondary school). It was assumed that all children would be entitled to NHS dental care until the age of 16 or 17 years, which would represent the ages of children up until the 10-year time horizon.⁵⁹

We assumed that children would continue to receive their original intervention (i.e. they would not receive both interventions) and that the same products would be applied in a similar way to that in the trial. The standard of application and the efficacy of the staff administering the intervention would be commensurate

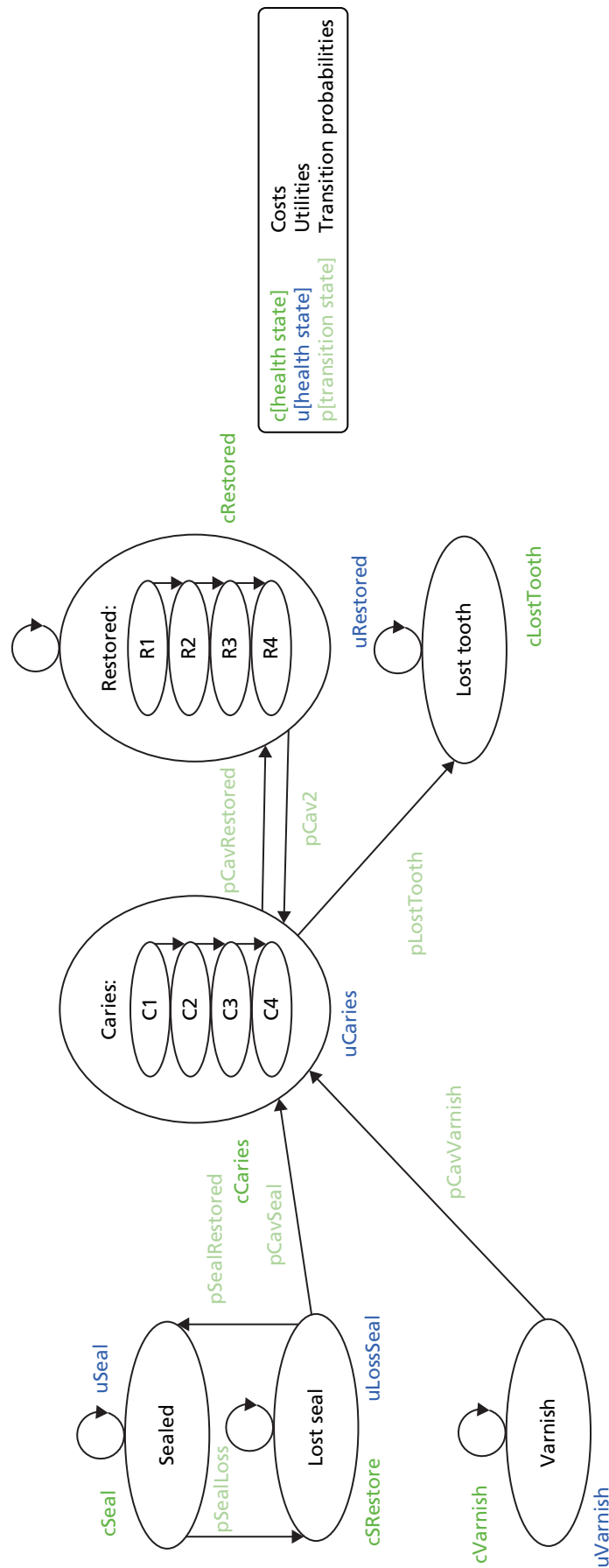


FIGURE 6 Markov state diagram: outline of modelled intervention pathways for FS vs. FV. The states are represented by ovals and possible transitions between states are represented by arrows.

with the trial, as would the accuracy in diagnosing and appropriately treating the tooth. For the base case, we assumed that children would visit a NHS community dentist and receive the intervention in accordance with standard practice, including, when required, the reapplication of FV or resealing of FS.

The trial permitted the child's tooth to be assessed to ensure that the FPMs were sufficiently erupted to be treated, as part of the early detection of caries risk provided by the MDC. The same dental recall periods were used within the first 5 years of the model, that is, periods of 6 months, as the child would still be in the Designed to Smile programme. Between 5 and 10 years, it would be assumed that the recall period would be based on an individual risk-based assessment for each child and thus it would be problematic to provide a precise estimate of the time interval. NICE guidance⁶⁰ recommended that the shortest interval for oral health reviews for all patients should be 3 months, and, for patients < 18 years old, the longest interval should be 12 months. The health economic analysis undertaken for this guideline used Markov-based modelling to assess the cost-effectiveness of different dental recall periods, emphasising that, with considerable uncertainty around model parameters (particularly clinical efficacy), conclusions about the relative cost-effectiveness of different recall times could not be drawn.

On the basis of the trial outcomes, and as agreed with the trial team, it was assumed that all children attended a dental visit every 6 months. This was assumed to be the same for both trial arms.

Within this model, no assumptions were made regarding the accuracy of clinical assessments or the impact of different clinical reversal rates and it was assumed that a similar reversal rate could be achieved as that in the trial results on caries progression. The possible impact of dental health problems (e.g. caries progression in other teeth) or other oral health interventions on the subsequent health states of the FPMs was not considered.

Base-case inputs

As this was a model developed from the SoV trial, when possible and appropriate, the clinical evidence from the trial, alongside the costs and outcomes used in the within-trial health economic analysis, were used to provide data inputs. The FS was the base case, with incremental cost-effectiveness reported for FV compared with FS.

Although the trial provided estimates of the incidence of caries at baseline and the rate of caries progression as a result of the two technologies up until 36 months' follow-up, it was problematic to estimate precise estimates of progression beyond the trial duration.

The strongest clinical evidence would be derived from the updated Cochrane review that evaluated the relative clinical effectiveness of FS versus FV (and FS + FV vs. FV alone) for preventing dental caries in the occlusal surfaces of permanent teeth of children and adolescents.¹⁶ From this review, only one study provided longer-term outcome data,⁶¹ which was assessed to have both an unclear risk of bias because no information was provided at 48 months, and a high risk of bias as only 33% of trial participants were included at 9 years' follow-up. This trial was also assessed as having a high risk of bias for four key domains (outcome assessment, incomplete outcome data, selective reporting and baseline comparability). The model was therefore constrained by using evidence from the trial, and discussions with the clinical trial team were used to make assumptions, when necessary. All data inputs underwent full validation by the trial team, and uncertainty was considered within the sensitivity analysis.

Clinical data

The trial data were used to inform the probability of the different progression into caries through the model.

Costs

It was assumed that modelled patients accrued costs associated with any assessment and intervention and that they continued to receive interventions to prevent/manage caries progression in the FPMs. The costs reflected a NHS and Personal and Social Services perspective, that is, drug costs, intervention costs and any other resource use that may be required (e.g. adverse events).

The same costing approach was used from the within-trial analysis of costs, valued in monetary (£) terms at 2015 prices from unit costs from published sources, for example BNF, Personal and Social Services Research Unit and NHS reference costs and, when applicable, local financial records from Cardiff and Vale UHB. *Tables 48 and 49* reported the costs utilised in the model.

Health utilities

The following estimates of QoL were used (*Table 52*), using the trial data to estimate utility decrements.

One-way sensitivity analysis

Table 51 presented the range of parameter estimates applied to the comparison of FS with FV in the one-way sensitivity analysis of the CUA, and these were applied to the model.

Probabilistic sensitivity analysis

A probabilistic sensitivity analysis was performed to test the robustness of the modelling conclusions in the face of uncertainty surrounding the choice of modelling inputs. Parameter values were varied within a reasonable range in each of 1000 runs and the results averaged across runs. Costs were sampled from gamma distributions, utilities from beta distributions, and rates and probabilities from log-normal or beta distributions. A CEAC was generated to depict the probability of the intervention being cost-effective at different willingness-to-pay (WTP) thresholds.

Results: within-trial analysis

Intervention costs

The interventions costs for FS versus FV are shown in *Table 53*. The overall intervention costs were aggregated across all the treatment and clinical assessment time points, as per the trial protocol. For the base case, the overall mean costs were lower for FV than for FS (£32,146.50 vs. £38,098.71, respectively). These were mainly attributed to the difference in time receiving treatment (in chair) between the two treatments. The overall time in chair across the trial period was 24 minutes for FS and 16 minutes for FV; even taking into account the reapplication of FV over the trial period, this cost of treatment remained lower (£74.12 per FS patient vs. £64.16 per FV patient). When the costs of the MDC were added, this increased the mean per-patient cost in each arm, but the incremental difference was small (£95.73 vs. £86.33 for FS vs. FV, respectively).

Dental visits

The DHQ was used to estimate the resource use over the 3 years based on all available data for the two interventions. Children in the FV arm had, on average, fewer visits to the dentist (outside the MDC) than children in the FS arm (3.5 vs. 3.9, respectively). However, there were small differences in the reasons documented for these visits, with more children in the FS arm than in the FV arm attending for 'check-ups' (3 vs. 2.7, respectively), which equates to a difference of £28 per patient across the arms. The estimated

TABLE 52 Base-case utility values used in the model-based analysis

	Value
QoL weight for one cycle of sealed tooth	0.002
QoL weight for one cycle of lost seal	0.002
QoL weight for one cycle of varnished tooth	1E-12
QoL weight for one cycle with dental caries	0.05
QoL weight for one cycle of restored tooth affected by dental caries	0.05

TABLE 53 Intervention costs of FS vs. FV

Basis of estimate	Unit cost (£)	Per hour (£)	Per full treatment (FS = 24 minutes), (£)	Per full treatment (FV = 16 minutes), (£)	Data sources
Dentistry staff band 3 × 1		9.20	3.68	2.45	NHS Staff Agenda for Change ⁴³
Dentistry staff band 4 × 1		10.58	4.23	2.82	NHS Staff Agenda for Change ⁴³
Dentistry staff band 5 × 0.65		12.62	5.05	3.37	NHS Staff Agenda for Change ⁴³
Administration staff (band 3) × 1		9.20	3.68	2.45	NHS Staff Agenda for Change ⁴³
Administration staff (band 4) × 1		10.58	4.23	2.82	NHS Staff Agenda for Change ⁴³
FV (Duraphat)	2.00			12.00	Dental supplier ^a
FS (Delton)	2.50		15.00		Dental supplier ^a
Clinical disposables (e.g. gloves, cotton wool, bib, etc.)	2.50		22.50	22.50	Dental supplier ^a
Sterilisation costs	1.75		15.75	15.75	Cardiff and Vale UHB ^b
Intervention costs total			38,098.71	32,146.50	–
Number of eligible pupils			514	501	–
Cost per eligible pupil			74.12	64.16	–

a www.henryschein.co.uk (accessed in March 2016).
b www.cardiffandvaleuhb.wales.nhs.uk/home (accessed in March 2016).

mean cost per patient associated with additional dental visits in the FS was £426, compared with £368 in the FV (£58.17, 95% CI –£4.33 to £120.67). The results are shown in *Table 54*.

An important cost driver to assess differences between the two technologies would be the treatment required as a result of caries within the FPMs, for example the cost of filling or removing the index tooth. One of the limitations of the DHQ is that it would not be precise enough to estimate direct costs attributed to the FPMs. Thus, the clinical trial data were examined to give a more accurate estimation of the costs of treating caries, assigning a cost to each event based on the unit cost of treatment. These were used as the primary source of data for these key cost drivers, with the DHQ providing information of other dental health-related events.

With regard to hospital visits (e.g. hospital-based dental outpatients) and hospital admissions associated with dental health problems, there were no recorded events across both treatment groups. No other health-care attendances were recorded (e.g. accident and emergency department attendance or out-of-hours service).

Prescription costs

Parents were asked to estimate the prescriptions given by a dentist or other health-care professional given to treat dental health problems during the trial. On examining the data, there were some anomalies noted, insofar as a prescription was recorded but not the prescribing health-care professional (e.g. dentist or general practitioner). This was discussed by the trial team and it was assumed that a community dentist would have prescribed. Painkillers and antibiotics were the only medications prescribed. It was assumed this was done as part of a dental visit already counted.

TABLE 54 Summary of resources utilised and associated with dental health problems

Resource	Intervention arm				FV				Difference			p-value	
	FS		FV		FV		FV		Mean	SD	Sum		
	Mean	n	SD	Sum	Mean	n	SD	Sum					
Number of appointments per patient	3.9	514	3.3	2024	3.5	501	3.3	1772	-0.4	-0.1	-252	0.40 (-0.01 to 0.81)	0.053
Cost of appointments per patient	£425	514	£523	£218,680	£367	501	£490	£183,920	-£58	-£32	-£34,760	58.34 (-4.14 to 120.82)	0.067
Number of painkillers administered per patient	0.07	514	0.52	37	0.13	501	0.64	67.00	0.06	0.12	30.00	-0.06 (-0.13 to 0.01)	0.090
Cost of painkillers administered per patient	£0.01	514	£0.10	£7	£0.03	501	£0.12	£13	£0.01	£0.02	£6	-0.01 (-0.03 to 0.00)	0.090
Number of antibiotics administered per patient	0.11	514	0.50	54	0.17	501	0.71	84	0.06	0.20	30	-0.06 (-0.14 to 0.01)	0.104
Cost of antibiotics administered per patient	£0.26	514	£1.26	£135	£0.42	501	£1.77	£210	£0.16	£0.51	£75	-0.16 (-0.35 to 0.03)	0.104
Combined prescription costs per patient	£0.28	514	£1.28	£142	£0.44	501	£1.85	£223	£0.17	£0.57	£81	-0.17 (-0.36 to 0.03)	0.091
Total cost to the NHS	£426	514	£523	£218,822	£368	501	£491	£184,143	-£58.17	-£32.34	-£34,679	58.17 (-4.33 to 120.67)	0.068
Cost of time off work to parent/carer	£29	514	£27	£14,799	£25	501	£26	£12,508	-£4	-£1	-£2291	3.83 (0.55 to 7.10)	0.022
Total cost to parent/carer	£29	514	£27	£14,799	£25	501	£26	£12,508	-£4	-£1	-£2291	3.83 (0.55 to 7.10)	0.022
Total combined NHS and parent/carer costs attributable to dental appointments alongside intervention	£455	514	£542	£233,621	£393	501	£508	£196,650	-£62	-£33.27	-£36,970	62.00 (-2.75 to 126.75)	0.061
Intervention cost per patient	£74.12	514	-	£38,098.71	£64.16	501	-	£32,146.50	-£9.96	-	-	-	-
Total cost to the NHS and intervention costs	£500	514	£523	£256,920	£432	501	£491	£216,287	-£68	-£32.34	-£40,633	-68.13 (5.63 to 130.63)	0.033
Overall costs (including intervention costs)	£529	514	£542	£271,718	£457	501	£508	£228,794	-£71.96	-£33.27	-£42,924	-71.96 (7.21 to 136.71)	0.029

The estimated mean per-patient cost for medications prescribed in the FS arm was £0.28, compared with £0.44 in the FV arm (−£0.17, 95% CI −£0.36 to £0.03). This was seen as a non-statistically significant difference (see *Table 53*; $p = 0.091$).

The base-case analysis shows that the children randomised to the FS arm accumulated more costs, overall, than children in the FV arm. *Table 54* also shows the comparison of total mean health-care costs between the two technologies. These results were used in the subsequent cost-effectiveness analyses and budget impact analysis.

Costs to the family

The costs to the family were estimated from the DHQ. With regard to over-the-counter medications, the total costs were £12.54 for FS versus £13.49 for FV. In terms of carer time as a result of taking time off to attend dental health appointment with the participating child or time to look after the child, the mean per-carer cost was estimated to be £29 versus £25 for FS versus FV, respectively. *Table 54* shows the costs to the family regarding the costs resulting from time off.

Cost of hosting mobile dental clinic to the school

The schools questionnaire was returned by 30% of the participating schools. In their responses, all schools stated that there were negligible costs associated with the school's participation related to the MDC, with little disruption to classroom time for the teacher or administrative tasks. Thus, the costs to the school of hosting the service were not formally analysed.

Overall NHS costs

Table 54 shows the health-care contacts across the trial arms from the NHS perspective. Non-statistically significant differences were seen in the contacts, that is, £425 versus £367 (FS vs. FV, respectively), with a difference of £58.17 (95% CI −£4.33 to £120.67; $p = 0.068$).

Total combined NHS and family costs

Table 54 shows the health-care contacts across the trial arms from the perspective of the NHS and a partial societal (family) perspective. Statistically significant differences were seen in the 'total cost of time off work' contacts, that is, £28.79 versus £24.97 (FS vs. FV, respectively), a difference of £3.83 (95% CI £0.55 to £7.10; $p = 0.022$).

The costs of the two technologies showed small but statistically significant differences; the mean cost to the NHS (including intervention costs) per child was £500 for FS, compared with £432 for FV, a difference of £68.13 (95% CI £5.63 to £130.63; $p = 0.033$) in favour of FV.

When costs to the family were included (with NHS costs), the costs were £529 for FS and £457 for FV, with a difference of £71.96 (95% CI £7.21 to £136.71; $p = 0.029$) in favour of FV.

Health outcomes

Dentine caries avoided at 36 months

The data presented in *Table 13* were used to estimate the cost of each 1% reduction in the proportion of children who at 36 months had developed dental caries.

Health utilities and quality-adjusted life-years

The mean utility values derived from the CHU-9D at each of the follow-up points were similar (p -values greater than 0.05) for both technologies (*Table 55*). In the FS arm, the mean utility value (and resultant QALY) was 0.928 at 12 months and this increased to 0.933 at 36 months. In the FV arm, the mean utility value (and resultant QALY) was 0.931 at 12 months and this increased to 0.933 at 36 months.

TABLE 55 Health utilities and QALYs by treatment arm

Treatment allocation	<i>n</i>	Mean (SD)	95% CI of the difference	<i>p</i> -value
CHU-9D 12 months				
FS	262	0.928 (0.072)	–0.003 (–0.015 to 0.009)	0.624
FV	248	0.931 (0.061)		
CHU-9D 24 months				
FS	272	0.926 (0.074)	–0.002 (–0.015 to 0.010)	0.720
FV	252	0.928 (0.069)		
CHU-9D 36 months				
FS	236	0.933 (0.066)	0.000 (–0.012 to 0.013)	0.956
FV	219	0.933 (0.066)		

The effects of these very small changes in the CHU-9D (both within and across the two arms) are reflected in the negligible utilities lost/gained and subsequent QALYs from 12 to 36 months. Overall, there was a small and non-statistically significant difference in QALYs at 36 months in the FV arm (0.931) compared with the FS arm (0.929) (difference 0.002, 95% CI –0.010 to 0.005). However, the very small difference and the 95% CIs indicate that these data should be treated with some caution (*Table 56*). In effect, there is a non-statistically significant difference and negligible clinically significant difference in QALYs, which was a similar result to the clinical outcomes reported in the trial.

Tooth utilities and quality-adjusted tooth-years

Table 57 reports the tooth utilities associated with the two technologies and QATY differences. The mean tooth utility at 36 months was 0.932 in the FS arm and 0.925 in the FV arm. The overall QATY difference was 0.007 in favour of the FS arm, a small and non-significant numerical difference. The clinical significance of this result is negligible and thus should be regarded with caution.

Cost-effectiveness analysis

Incremental cost per child with dentine caries avoided

The base case of the analysis for the incremental cost per child with dentine caries avoided is presented in *Table 58*.

TABLE 56 Health utilities and QALYs

Time period	Intervention arm				
	FS		FV		QALY difference
	CHU-9D score	Change over time	CHU-9D score	Change over time	
12 months	0.928	–	0.931	–	–
24 months	0.926	–0.001	0.928	–0.001	–
36 months	0.933	0.004	0.933	0.002	–
QALY gain at 3 years	–	0.003	–	0.001	0.002 (–0.010 to 0.005)

TABLE 57 Tooth utilities and QATYs

Intervention				
FS		FV		QATY difference
Tooth	Tooth utility	Tooth	Tooth utility	
UR6	0.925	UR6	0.937	–
UL6	0.927	UL6	0.938	–
LR6	0.933	LR6	0.906	–
LL6	0.944	LL6	0.920	–
Overall FPM utility	0.932	Overall FPM utility	0.925	0.007 (–0.068 to 0.011)

LL, lower left; LR, lower right; UL, upper left; UR, upper right.

TABLE 58 Incremental cost per 1% of proportion of children with dentine caries prevented

Parameter	Incremental cost of intervention (£)	Proportion of children without dentine caries	ICER (using % dentine caries free scores)
Base case	–68.13 (–5.63 to –130.63)	0.021 (–0.0317 to 0.0738)	FV is dominant ^a
Upper 95% bound of net cost	–130.63	0.0738	FV is dominant ^a
Upper 95% bound caries free (%)			
Upper 95% bound of net cost	–130.63	–0.0317	FV is dominant ^a
Lower 5% bound of caries free (%)			
Lower 5% bound of net cost	–5.63	–0.0317	FV is dominant ^a
Lower 5% bound of caries free (%)			
Lower 5% bound of net cost	–5.63	0.0738	FV is dominant ^a
Upper 95% bound caries free (%)			

a With very small numerical differences in effect in favour of FV and FV being less costly than FS, the ICER is calculated as dominant. However, this calculation is based on non-statistically significant differences in outcomes between FS and FV.

With very small numerical differences in dental caries between the two trial arms, the ICER computed that FV was dominant over FS. However, appropriate caution should be exercised in using and interpreting the term ‘dominant’ in the context of these results.

Sensitivity analysis

As shown in *Table 58*, the results remained consistent when adjusted around the upper and lower range (95% CI) for costs and outcome. The CEAC for the incremental cost per child with dentine caries avoided is shown in *Figure 7*. Although there is no formal threshold, this illustrates the probability of FV being cost-effective at different monetary WTP thresholds.

Incremental cost per quality-adjusted life-year

Table 59 shows the incremental cost per QALY.

Figure 8 presents the CEAC.

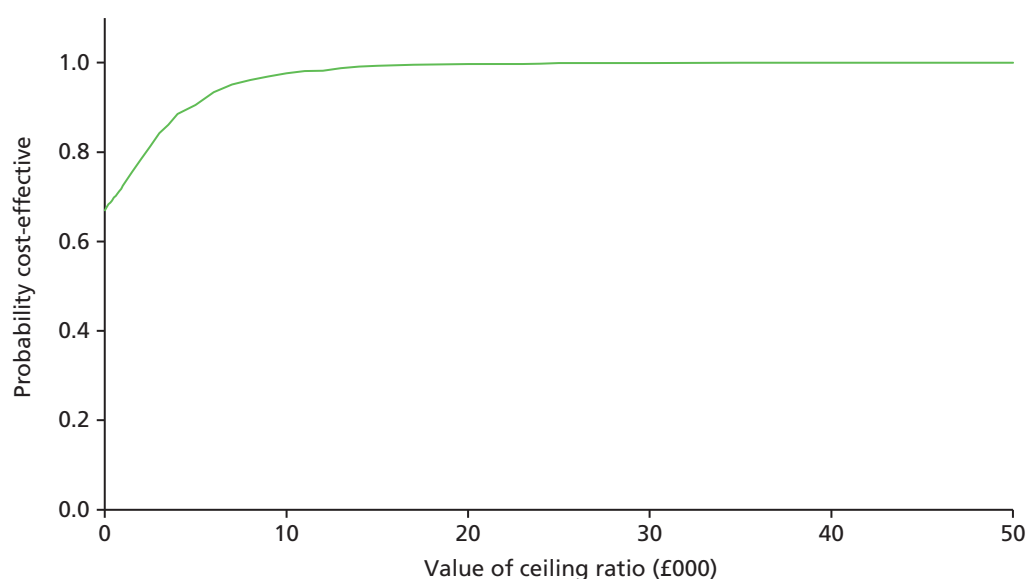


FIGURE 7 The CEAC for incremental cost per child with dentine caries avoided.

TABLE 59 Incremental cost per QALY

Parameter	Incremental cost of intervention (£)	Incremental CHU-9D utility	ICER (using CHU-9D utility scores)
Base case	-68.13 (-5.63 to -130.63)	0.002 (-0.010 to 0.005)	FV is dominant ^a
Upper 95% bound of net cost	-130.63	0.005	FV is dominant ^a
Upper 95% bound of net utility			
Upper 95% bound of net cost	-130.63	-0.010	FV is dominant ^a
Lower 5% bound of net utility			
Lower 5% bound of net cost	-5.63	-0.010	FV is dominant ^a
Lower 5% bound of net utility			
Lower 5% bound of net cost	-5.63	0.005	FV is dominant ^a
Upper 5% bound of net utility			

^a With very small numerical differences in effect in favour of FV and FV being less costly than FS, the ICER is calculated as dominant. However, this calculation is based on non-statistically significant differences in outcomes between FS and FV.

For the cost per QALY, the probability of FV being cost-effective is 70% at a NICE societal WTP threshold of £20,000 per additional QALY.

Incremental cost per quality-adjusted tooth-year

The base case of the analysis of the incremental cost per QATY is presented in *Table 60*. It can be seen that, in comparison with FV, FS generated slightly more QATYs. However, when the ICER calculation is performed, FV was dominant.

This is a result consistent with the previous ICERs, and the same caution is applied in the interpretation of these results. This remained consistent when a one-way sensitivity analysis was performed. As this was an exploratory analysis, no CEAC is presented.

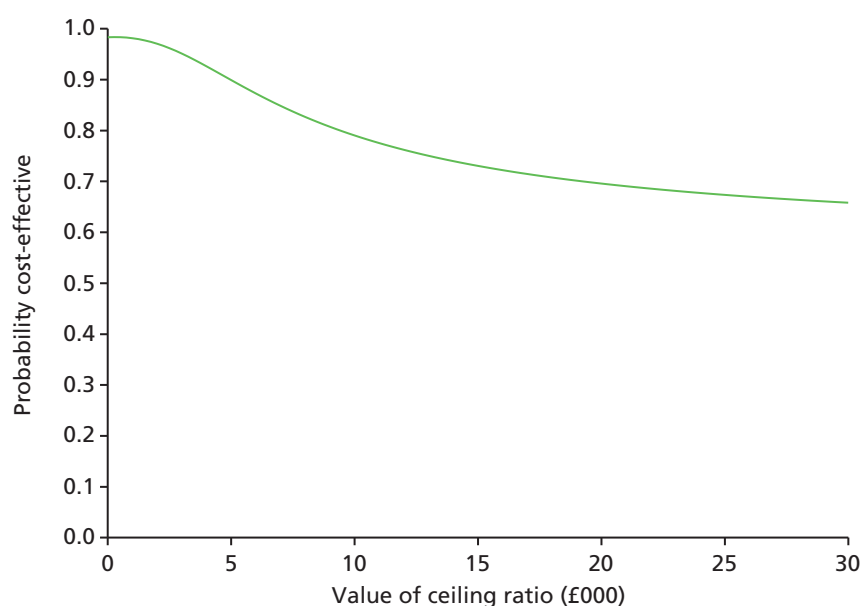


FIGURE 8 The CEAC (CUA).

TABLE 60 Incremental cost per QATY

Parameter	Incremental cost of intervention (£)	Incremental tooth utility	ICER (using tooth utility scores)
Base case	-68.13 (-5.63 to -130.63)	0.007 (-0.068 to 0.011)	FV is dominant ^a
Upper 95% bound of net cost	-130.63	0.011	FV is dominant ^a
Upper 95% bound of net utility			
Upper 95% bound of net cost	-130.63	-0.068	FV is dominant ^a
Lower 5% bound of net utility			
Lower 5% bound of net cost	-5.63	-0.068	FV is dominant ^a
Lower 5% bound of net utility			
Lower 5% bound of net cost	-5.63	0.011	FV is dominant ^a
Upper 5% bound of net utility			

a With very small numerical differences in effect in favour of FV and FV being less costly than FS, the ICER is calculated as dominant. However, this calculation is based on non-statistically significant differences in outcomes between FS and FV.

Budget impact analysis

The budget impact analysis (*Table 61*) was calculated on the trial population patients at 3 years ($n = 1015$). The total cost of FS treatment was £38,098 and the total cost of FV treatment was calculated at £32,144 (or £74.12 per patient in the FS arm and £64.16 per patient in the FV arm). The NHS costs associated with dental appointments (other than those administered in the intervention) totalled £218,822 for the FS arm and £184,143 for the FV arm. When the costs of implementation and the resource usage costs are combined and compared between arms, there is a -£35,021 cost-saving difference in favour of FV over the trial period. The results show that there is an overall per-patient cost saving of £68.13 (95% CI £5.63 to £130.63; $p = 0.033$) in favour of the FV arm compared with the FS arm.

TABLE 61 Budget impact analysis at 3 years based on trial population

Baseline	Intervention arm	
	FS	FV
Cost of implementation (£)	38,098	32,144
Number of patients	514	501
Cost of implementation per patient (£)	74.12	64.16
Total cost of dental appointments (£)	218,822	184,143
Mean cost of dental appointments per patient (SD)	425.7 (523.0)	367.5 (490.6)
Difference (95% CI)	-58.17 (-4.33 to 120.67)	
Overall cost differences between the interventions (£)	-35,021	
Cost saving per patient (£)	-68.13	

Sensitivity analysis of the budget impact analysis

Deterministic sensitivity analyses were conducted to estimate the worst-case and best-case scenarios of the budget impact of FS versus FV by using the lower and upper costs derived from the trial. To examine different scenarios that could impact on NHS budgets, three additional scenarios were explored: (1) the budget impact when the costs of the MDC are included, (2) the budget impact of a community dental nurse delivering FV in a 'classroom' setting (i.e. not requiring a MDC but reflecting potential for this technology to be delivered in a single application with minimal equipment/resources), and (3) the budget impact when a dental hygienist alone applies FV within a classroom/school medical room setting.

Table 62 shows the different cost scenarios for the intervention over a 3-year period as seen in the trial. It can be seen that the deterministic sensitivity analysis is unchanged in most of the modelled scenarios, that is, FV is dominant and is seen to be the optimal strategy. However, when the best-case cost scenario of £51.88 for FS is compared with the worst-case cost scenario of £83.41 for FV, FS technology dominates. That FS could cost as little as this in a real-life setting is questionable, and so caution should be exercised with regard to this. Further work would be required to explore the plausibility of this scenario.

TABLE 62 Base-case and sensitivity analysis of the cost of delivering the technologies in the school setting using best-case/worst-case scenarios

Parameter	Intervention arm		Budget impact
	FS	FV	
Base case (lower ranges, upper ranges)	74.12 (51.88, 96.36)	64.16 (44.91, 83.41)	FV is dominant
Upper range FS	96.36	83.41	FV is dominant
Upper range FV			
Upper range FS	96.36	44.91	FV is dominant
Lower range FV			
Lower range FS	51.88	44.91	FV is dominant
Lower range FV			
Lower range FS	51.88	83.41	FS is dominant
Upper range FV			

Table 63 shows the different cost scenarios for the intervention to be administered if the costs of the MDC are included. It can be seen that the deterministic sensitivity analysis is unchanged in most of the modelled scenarios, that is, FV is dominant and is seen to be the optimal strategy. However, when the best-case cost scenario of £67.01 for FS is compared with the worst-case cost scenario of £112.23 for FV, FS dominates. The plausibility of this scenario reflecting a real-life cost needs further discussion.

Table 64 represents the analysis of one FV application by a dental nurse in the school. It can be seen that, by reducing the costs of the FV technology, it becomes dominant and is seen to be the optimal strategy across all the scenarios. The plausibility of this scenario reflecting a real-life cost would need further investigation.

Finally, Table 65 represents the analysis of one FV application by a dental hygienist in the school. Again, it can be seen that, by reducing the costs of the FV technology, it becomes dominant and is seen to be the optimal strategy across all of the scenarios. Again, the plausibility of this scenario reflecting a real-life cost would need further investigation.

TABLE 63 Base-case and sensitivity analysis of the cost of delivering the technologies in the school setting (with additional MDC costs included) using best-/worst-case scenarios

Parameter	Intervention arm		Budget impact
	FS	FV	
Base case (lower ranges, upper ranges)	95.73 (67.01, 124.45)	86.33 (60.43, 112.23)	FV is dominant
Upper range FS	124.45	112.23	FV is dominant
Upper range FV			
Upper range FS	124.45	60.43	FV is dominant
Lower range FV			
Lower range FS	67.01	60.43	FV is dominant
Lower range FV			
Lower range FS	67.01	112.23	FS is dominant
Upper range FV			

TABLE 64 Deterministic sensitivity analysis of the FV application by a dental nurse in the school (classroom or medical/school nurse room setting)

Parameter	Intervention arm		Budget impact
	FS	FV	
Base case (lower ranges, upper ranges)	74.12 (51.88, 96.36)	11.48 (8.04, 14.92)	FV is dominant
Upper range FS	96.36	14.92	FV is dominant
Upper range FV			
Upper range FS	96.36	8.04	FV is dominant
Lower range FV			
Lower range FS	51.88	8.04	FV is dominant
Lower range FV			
Lower range FS	51.88	14.92	FV is dominant
Upper range FV			

TABLE 65 Deterministic sensitivity analysis of the FV application by a dental hygienist in the school (classroom or medical/school nurse room setting)

Parameter	Intervention arm		Budget impact
	FS	FV	
Base case (lower ranges, upper ranges)	74.12 (51.88, 96.36)	10.91 (7.64, 14.18)	FV is dominant
Upper range FS	96.36	14.18	FV is dominant
Upper range FV			
Upper range FS	96.36	7.64	FV is dominant
Lower range FV			
Lower range FS	51.88	7.64	FV is dominant
Lower range FV			
Lower range FS	51.88	14.18	FV is dominant
Upper range FV			

Additional scenario analysis

To provide further illustration of the practical implications of the findings, an additional scenario analysis was undertaken to provide a hypothetical illustration of the time savings that could be achieved in delivering FS versus FV. As shown in the results, one of the resources attributed to costs is the 'time in chair' and another is the skill mix of staff that would be needed to deliver the technologies and how these findings can be used to optimise capacity and the number of children treated within the service. The ideal service configuration of preventative dental health for a population of children at high risk of caries is informed by translating the time savings gained from using FV with a dental care team that, compared with FS, needs to be less highly trained and does not include a qualified dentist. *Table 66* presents an illustrative scenario (using time to treat each child gathered from the trial) in which, compared with FS, using FV allows 93 more children to be treated within the same time (assuming a day's session, based on the school working day of 9 a.m. to 3 p.m., at a school that has this number of children).

Post-trial modelling

Table 67 reports the estimations of the incremental cost per QALY at 5 and 10 years. These base-case results estimate that FV continues to be dominant over FS because of lower costs and slightly more QALY gains.

The results of the univariate sensitivity analysis estimated that FV remained dominant.

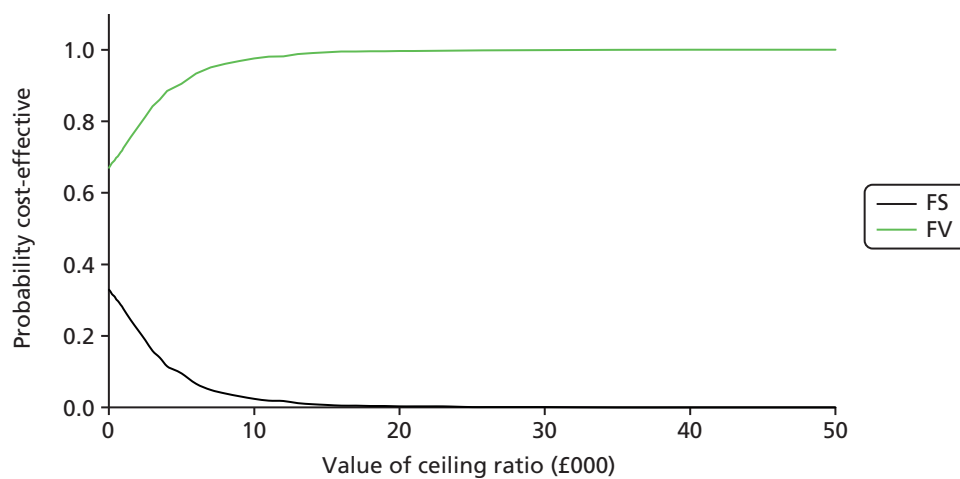
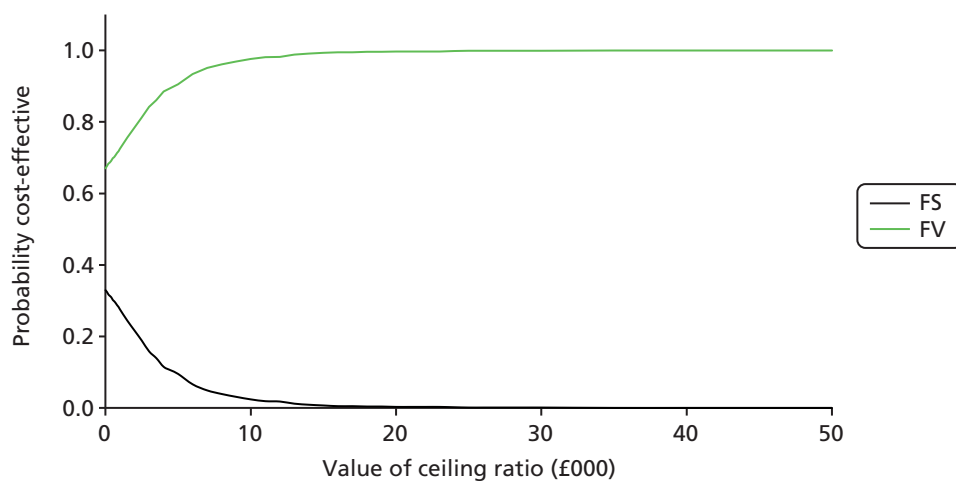
Figures 9 and *10* show the CEACs generated for 5 and 10 years, respectively. They show that, at a NICE societal WTP threshold of < £20,000 per QALY gained, FV is 99% (at 5 years) and 96% (at 10 years) likely to be cost-effective.

TABLE 66 Illustrative scenario of hypothetical time savings that could be achieved between delivering FS versus FV

	Intervention arm		Difference
	FS	FV	
Average time of one application of FV (minutes)	–	2.7	–
Average time per patient for one-off treatment of FS (with no top-ups)	8.9	–	–
Number of minutes in a session (9 a.m. to 3 p.m.)	360	360	–
Theoretical number of patients to be seen per session	40	133	93

TABLE 67 Incremental cost per QALY at 5- and 10-year horizons

	Cost (£)		Incremental cost (£)	QALY		Incremental QALY	ICER
	FS	FV		FS	FV		
5 years	1055	663	391	0.03	0.15	-0.12	FV is dominant
10 years	1580	822		0.05	0.31	-0.26	FV is dominant

**FIGURE 9** The CEACs for a 5-year time horizon.**FIGURE 10** The CEACs for a 10-year time horizon.

Summary of health economic results

This chapter has reported the health economic methods and findings of the trial. The main findings are as follows.

- It is feasible to undertake a comprehensive health economic evaluation alongside a randomised controlled trial of preventative health technologies within in the context of a MDC setting.
- The intervention costs of the two technologies were £74.12 (FS) and £64.16 (FV) per child over the course of the trial.
- The costs of the two technologies showed small but statistically significant differences between arms; the mean cost to the NHS (including intervention costs) per child was £500 for FS compared with £432 for FV, a difference of £68.13 (95% CI £5.63 to £130.63; $p = 0.033$) in favour of FV.
- When a partial societal perspective was included (with intervention costs), the mean cost per child was £529 for FS and £457 for FV, a difference of £71.96 (95% CI £7.21 to £136.71; $p = 0.029$) in favour of FV.
- The budget impact analysis at 3 years showed that FV had a cost saving of £68.13 (95% CI £5.63 to £130.63; $p = 0.033$) compared with FS. In addition, when three different scenarios were examined, the results did not change and FV remained dominant.
- As numerical differences in outcomes were non-significant, the ICER was very sensitive to very small numerical differences in outcomes. For all outcomes, differences between FS and FV were neither statistically significant nor clinically important, and so the ICER calculation should be treated with appropriate caution. However, results remained consistent across all three outcomes used in the health economic analysis, that is, FV was less costly than FS, with similar outcomes achieved.
- The CEAC showed that there was a 70% probability of FV being cost-effective at a societal WTP threshold of £20,000 per QALY.
- The results of model-based analysis to estimate the incremental cost per QALY over longer-term horizons were consistent with the results of the in-trial analysis, with FV being associated with lower costs and small QALY gains achieved, leading to FV being dominant in the ICER calculation. The CEACs showed that there was a 99% (over 5 years) and 96% (over 10 years) probability of FV being cost-effective within a societal WTP threshold of £20,000 per QALY. However, there are a number of uncertainties in the model, particularly the dearth of evidence on longer-term costs and outcomes associated with FV and FS within a preventative dental health context.

Chapter 5 describes the process evaluation.

Chapter 5 Acceptability of the Seal or Varnish? intervention and trial

Introduction

An important element of the clinical trial was determining the acceptability of the interventions provided, and the setting in which they were being provided, from the perspective of the participating children, their parents, schools/school staff and clinical staff. In addition, parents' decisions and perceptions of their child participating or not participating in the trial were investigated. A mixed-methods approach was used.

Treatment acceptability was assessed in three ways:

1. Acceptability scales were completed by clinical staff.
2. Acceptability scales also were completed by the children participating in the trial.
3. Qualitative interviews were conducted with a subsample of children.

A longitudinal process evaluation for the trial was conducted to assess how the FS/FV intervention was implemented for children in a school-based setting in a socioeconomically deprived area and to facilitate the interpretation of outcome effects to establish what works for whom and in what circumstances. The process evaluation focused on implementation and acceptability, as these were factors likely to influence the effectiveness of the trial, in addition to treatment efficacy. The research questions addressed and the mode of data collection are shown in *Table 68*.

The methods used were, briefly, the completion of acceptability scales by treating clinicians and the participating children, interviews conducted with participating children and their parents, interviews with head teachers of schools participating in the study and interviews with CDS staff delivering treatment. Parents who were not participating in the trial were also interviewed. In addition, a school staff questionnaire was sent to schools, and a short questionnaire about reasons for non-participation was included in the second recruitment mailing to parents for completion by parents who did not want to take part in SoV.

The methodology used is described in detail in *Methodology*. Findings on the acceptability of the intervention to children, parents, staff and schools are then reported. Any changes in oral health behaviour were also noted, to assess whether or not there were differences between trial arms that might affect outcomes. Reasons for parents consenting or not consenting for the children to participate in SoV are then described.

Methodology

Data collection

Acceptability as determined by observed signs of distress during treatment

An observation scale (see *Appendix 16*) was completed independently by the dental hygienist and dental nurse for each child immediately following application of the FS or FV. This scale recorded five items of children's behaviour: vomiting, crying, gagging, excessive arm/leg movements and other signs of distress.²⁹

Acceptability as reported by participants immediately following treatment

A DTF scale^{27,28} was used to assess the acceptability of the treatment for children, both for overall acceptability (how they felt during treatment and how they would feel if they had to have the treatment the following day) and for three specific aspects of treatment: taste, length of treatment and feeling sick (see *Appendix 12*).

TABLE 68 Summary of process evaluation research questions and data collection methods

Research question	Data collection method	Year of study in which data were collected		
		1	2	3
Acceptability: are FV and FS treatments acceptable to children aged 6–10 years, what factors influence acceptability and are there differences between trial arms? Includes:	Hygienist/nurse observation	X	X	X
	DTF scale	X	X	X
	Child interviews	X		X
Did the children display signs of distress during the treatment?	Parent interviews	X		X
	Clinician interviews	X	X	X
Did the children feel happy or sad after the treatment was completed?				
Implementation: is the delivery of this type of preventative treatment acceptable to children, their parents, clinicians and the schools where the treatments take place; what are the factors affecting implementation of treatment in a school setting?	Child interviews	X		X
	Parent interviews	X		X
	Clinician interviews	X	X	X
	School staff questionnaire	X		
	School staff interviews			X
What factors affect whether parents consent or do not consent to take part in an intervention and trial such as SoV?	Parent interviews	X		X
	Parent questionnaire	X		
	School staff questionnaire	X		
	School staff interviews			X
Does treatment with FV or FS affect (self-reported) subsequent oral health behaviour, and, if so, are there differences between trial arms?	Child interviews	X		X
	Parent interviews	X		X
What is the effect of the trial on recruitment or acceptability to parents, dental staff and schools?	Parent interviews	X		X
	Clinician interviews	X	X	X
	School staff interviews			X

As there are few scales designed for acceptability of dental treatment, and as none was available for very young children, the DTF scale was selected, but it was adapted by graphic artists to enhance visual appeal, as the original scale was designed for slightly older children. The DTF scale was completed by children in the MDC immediately following the initial application of FS/FV and at each follow-up visit. Answers were given on a five-point Likert scale, on which children could mark a picture of a face, which ranged from smiling to sad, to indicate how they felt about different aspects of treatment. The protocol for completion of the scale was for the child to sit apart from other children, to avoid children discussing or influencing each other's answers.

Interviews with children

School sampling

A subsample of schools participating in the trial was selected for acceptability interviews with children. All schools were in Communities First areas, which were characterised by deprivation; however, within this category there was a range of deprivation levels in schools. As the impact of preventative dental interventions in deprived areas was an area of interest for the study, the impact of level of deprivation was also of interest.^{5,6} Schools were selected from the highest and lowest deprivation quartiles of schools in the SoV trial, measured by the percentage of pupils in a school receiving free school meals (FSMs). Data were used from the StatsWales website of the Welsh Assembly Government,⁶² and the measure used was the percentage of 5- to 15- year-olds eligible for FSMs in 2010. The overall range of children receiving FSMs in

participating SoV schools was 3–75%. The high-deprivation quartile schools had an average FSM rate of 58%, while the low-deprivation quartile schools had an average FSM rate of 18%. In the UK, the proportion of children receiving FSMs averages 15% across all schools, while the Welsh average is 18%. The sampled 'low-deprivation schools' in the SoV trial were, therefore, similar to the Welsh average, while the high-deprivation schools within the SoV trial had much higher levels of children receiving FSMs, at 58%, more than three times the average level of FSMs in Wales.

In year 1 of the study, schools with more study participants (either larger schools or smaller schools with high study consent rates) in each selected quartile were sampled for interviews. Schools were selected in this way to allow for large enough groups of children in each school to be paired by trial arm and also by children's choice of interview partner (see below). When numbers did not reach 24 for each trial arm, additional schools were added until at least 24 children had been interviewed in each trial arm. Because of problems contacting parents to gain consent for follow-up interviews in year 3, additional schools were sampled in year 3 to increase the sample size. The attempts to recruit for interview were stopped when around 30 children and parents had been interviewed. As respondents were providing similar answers and no new data were emerging from subsequent interviews, it was concluded that data saturation had been reached. Four schools were sampled in year 1 of the study; seven schools (including the four from year 1) were sampled for follow-up in year 3.

Child interview pairings

Children were interviewed in pairs, or occasionally singly or in threes, so that they would feel more comfortable in the interview environment.⁶³ The intention was also to facilitate the collection of more, and better-quality, data. Teachers and classroom assistants, and sometimes head teachers and school administrators, assisted with pairing children. Lists of children (identified by unique ID study number) participating in treatment for each school were divided by trial arm and, whenever possible, children from the same trial arm were interviewed together in order that children would be able to report on the same type of treatment in an interview. Within the trial arm groups, children were given the option to choose their interview partner (or teachers were asked to pair children with a friend). In some cases, the requirements of teachers or classroom activities also dictated which children would accompany each other, particularly when a year group was split over two or three classrooms. Originally, children were also to be purposively sampled from each trial arm for a range of acceptability scores, and children in each trial arm with similar acceptability scores were to be interviewed together, to ensure a maximum difference of acceptability across the sample. However, this proved impossible, as the sample sizes for each trial arm in each school were too small to divide the children into further groups; it would have disrupted classes too much to create a very rigid list of pairings of children, and it would have prevented children from being able to choose their interview partner.

Child interviews

Face-to-face paired interviews were conducted with children in a school setting ≤ 2 weeks after their first treatment and ≤ 2 weeks after their final treatment, to ensure that children's recall of their experience of treatment was reasonably accurate. Most children were interviewed within a few days of their treatment. Interviews lasted for around 15–20 minutes each and most children appeared relaxed and confident in interviews. Written parental consent to interview children was included in the main study consent; in addition, a reminder telephone call was made to parents in years 1 and 3 of the study to confirm consent before the researcher visited schools. Interviews were undertaken by one of the coauthors (SMT) and took place in spare classrooms, head teacher offices, staff rooms, school libraries and school halls. All interviews took place where school staff or other children could not hear the content of an interview (although, to comply with safeguarding requirements, all spaces were also visible) and it was explained to the interviewed children that the data collected were confidential. Assent to be interviewed was also verbally checked with children at the beginning of the interview. The interview topics included acceptability of treatment and the treatment setting, social influences on attitudes towards treatment and treatment settings (such as prior experience of dental treatment), changes in the child's oral hygiene behaviour and perceptions of treatment impact. See *Appendix 17* for the children's interview schedule. Fifty children were interviewed in year 1 of the study. Thirty-two follow-up interviews were conducted with children in year 3.

Methodological issues in child interviews

The children, especially in year 1 of the study when they were aged 6 or 7 years and at a relatively early developmental and educational stage, were limited in what they were able to report in interviews. Not all of the children were able to understand or to answer all of the questions posed in the interviews, and when the children were unable to answer a question, further probing questions were used in a very limited way to avoid causing anxiety. Several common limitations emerged across the group. First, some of the children's concepts of time were distorted; for example, one child in the final year of the study (when the children were 8 or 9 years old and the study was in its third year) thought that he had been receiving the treatment for about 8 years and then corrected himself and said it was only about 5 or 6 years. Most children in the first year of the study struggled with describing behaviour before and after a past event (e.g. 'have you changed how you brush your teeth since your last visit to the dental van?'). Their awareness of factors such as family and friends' dental habits was also limited, so social influences on their attitudes towards dental treatment were not always clear. They were not always able to be clear about the FS/FV treatment visits to the MDC, other visits to a MDC (e.g. examination visits for the study were also held in the MDC) and visits to a community dentist in town, especially in year 1 of the study. For example, children occasionally described a dental examination visit or having their teeth removed rather than a FS/FV treatment visit. They were also sometimes unable to consolidate or clearly articulate their feelings about an aspect of treatment, giving contradictory answers in interviews; this is not uncommon in qualitative interviews, but it occurred to a greater degree in the child interviews. Some children may have contradicted themselves in order to agree with their interview partner. When contradictory comments were made, data are not reported, as the child's preferences or views were not clear. Therefore, the number of unambiguous answers for each question or theme (such as whether or not children liked the taste of the treatment) reported here is lower than the number of children interviewed.

Interviews with participating parents

The interviews with parents were conducted by telephone 4–6 weeks after their child's first and last treatments, in years 1 and 3 of the study. Parents were interviewed after their children had been interviewed.

The interview schedule was piloted with parents at a local community centre in South Wales in an area that was not part of the trial. The following comments were received.

- The term 'interview' was perceived as intimidating. Parents preferred the terms 'courtesy call' or 'chat'. However, because there was a need to be clear to study participants that data were going to be collected and analysed, the term 'interview' was retained, but simpler language was used when parents were contacted. For example, parents were told that the purpose of the interview was to find out what they thought about SoV.
- Similarly, parents thought that 'recorded' sounded less ominous than 'tape-recorded', because 'recorded' sounded similar to the phrase 'your call may be recorded for training purposes', which people were used to hearing.
- Parents also suggested clarifying that interviews would take place by telephone; they said that this would encourage more parents to consent, as it was perceived as easier to participate in a telephone interview than in a face-to-face interview.
- Parents also made recommendations about recruiting other parents, suggesting that schools could be more involved in this. They suggested using posters with pictures to remind parents about the study and to increase trust because recruitment would be through the school. They also suggested enabling parents to collect and return forms directly to the school rather than by a postbox, especially to class teachers, as they are particularly trusted. Using plain English on posters and advertising, and clarifying that assistance from staff was available for parents with low literacy/English language skills, were also suggested as ways to increase accessibility.

Schools were not asked to assist further with recruitment as there were concerns about the research burden. Nevertheless, some schools did assist with recruiting. For example, one school inserted a reminder about study recruitment into the school newsletter, and one head teacher spoke to parents as a group about the trial, as he thought that the parents would not understand the paperwork.

Forty-nine parents were interviewed in year 1 of the study and 30 parents were interviewed in year 3. The aim of the interviews in year 3 was to follow up all interviewees from year 1; attempts were made to follow up as many children and parents from year 1 as possible, even if the child and parent could not be interviewed. The most common reason for not following up a child or parent was that the parent had changed their telephone number or did not answer the telephone despite several calls (the initial telephone call was partly to reconfirm consent, so if the parent was not contactable then their child was not interviewed). Another problem was the poor coverage of mobile phone reception in some areas of the South Wales valleys (many parents did not have landlines). Furthermore, telephone calls from the university were routed through the university switchboard; this resulted in the recipients of calls not being able to identify the caller number, which probably resulted in some parents not answering. A mobile phone was not a viable alternative because it could not be used in conjunction with a voice recorder for the interviews, and the reception/quality of the line tended to be poor. Three parents were followed up after the school was contacted for an up-to-date telephone number (permission to do this had been obtained in the study consent forms). Secondary reasons for not following up were that a few children were absent on the day of the interview at the school or had been withdrawn from the trial. As a result of the absent children and the various problems recontacting parents, follow-up in year 3 of the study with some parents and children was not possible. The intention was to interview the same pairs of parents and children in years 1 and 3; this was achieved for 17 child–parent pairs. To increase the overall number of interviews, additional schools were sampled and children and parents from these schools were also interviewed.

The interviews with parents were relatively short, lasting approximately 10–15 minutes, owing to parents' brief answers and often busy schedules; on some occasions, during the interviews, young children could be heard in the background. The interview topics included the acceptability of the treatment and the treatment setting, social influences on attitudes towards treatment and treatment settings (such as prior experience of dental treatment), changes in the child's oral hygiene behaviour, the perceptions of treatment impact and the acceptability and impact of the trial processes. See *Appendix 18* for the parent interview schedule.

Questionnaire and interviews with school staff

In year 1, a questionnaire was sent by e-mail to all 65 schools participating in the study. A second e-mail was sent to non-responding schools and, if required, further contact was made by sending postal questionnaires to any schools that had still not responded. The questionnaire included both closed and open questions about schools' experiences of the implementation of SoV (both the treatment programme and the trial) and acceptability of the intervention. Twenty-four questionnaires (37%) were returned.

In the third year of the trial, at the end of the school year, the 24 schools that had returned a questionnaire in year 1 were contacted by telephone to request their participation in an interview; those that agreed were sent consent forms to complete. Of the 24 schools contacted, five agreed to take part in an interview, and four interviews were actually conducted (one was cancelled because of sickness). Three interviewees were head teachers and one was a class teacher. The interviewees were asked about the impact of the trial and treatment delivery in the school, contextual factors that affected the feasibility and acceptability of delivering preventative treatment in a school setting, the acceptability of treatments and the recruitment of hard-to-reach parents for interventions. The interview schedule is in *Appendix 19*. The original intention had been to purposively sample schools based on their questionnaire responses; however, as only 24 questionnaires were returned in year 1, and as the sample of teachers or head teachers willing or able to spare time for an interview was likely to be only a fraction of this figure, all 24 schools were contacted so that the number of staff interviewed would not be too small.

Interviews with community dental unit staff

The dental team delivering the treatment was interviewed annually; this took place at the end of the school year. These interviews were conducted face to face at the CDS offices in Cardiff. Nine staff were interviewed in the first year and 12 staff were interviewed in both the second and the third years. This group included hygienists, dental nurses and the staff members who collected children from the

classrooms. The staff makeup of the groups was largely the same each time, but there were occasional omissions or additions because of staff leaving or joining, or because a staff member was unavailable (e.g. through sickness) on the days of the interviews. The interviews explored the feasibility and acceptability of delivery in a school setting, perceptions of acceptability of the treatment for children, child co-operation and perceptions of parent recruitment issues. The interview schedule is in *Appendix 20*.

Questionnaire and interviews with non-participating parents

For the first and second cohorts, the interviews with parents who did not participate in the trial were conducted after the trial recruitment periods had ended; this was to avoid any confusion or perceptions of harassment about recruitment to the trial itself rather than to a research interview. Two recruitment methods were used; the intention was to recruit up to 20 parents by each method. In the first method, if parents had not responded to the initial SoV recruitment attempt, they were sent information about the trial a second time. This information included a consent form for a telephone interview to discuss their reasons for non-participation, and a one-page questionnaire about their reasons, for those parents who did not wish to participate in the SoV study but were willing to take part in research about non-participation. The parents were invited to return the questionnaire, the consent form or both if they did not wish to participate in the trial. Those who returned the consent form were followed up with a telephone interview.

The second recruitment method was speaking to parents who had not returned any paperwork for the SoV trial itself and had also not returned the questionnaire or consent form for the interview about non-participation. This was done to collect data from parents who may have been willing to take part in the research but were unlikely to respond via a written invitation. Direct contact, including face to face, is likely to be effective for recruitment for interviews for hard-to-reach groups that have difficulty with literacy or paperwork and has the added benefit that a researcher visiting schools in person can familiarise people with a study and reduce anxiety about particular elements. It was also expected that teacher and school staff support for an intervention would have a positive influence on recruitment rates.⁶⁴ Seven schools were visited to recruit this group of parents and these were sampled by identifying schools that had lower than average recruitment rates for SoV, although very small schools were excluded as there were too few potential interviewees. The initial plan was to recruit parents from a parents' evening at a sample of schools, at which teachers and school staff would introduce the researcher to groups of parents and request participation in a research interview, but the research team was advised by several schools that it would be difficult because of how busy these events are and that parents would have limited time for interviews. Therefore, a second approach was devised.

In this second approach, a researcher waited with the year 2 class teacher by the exit door at the end of the school day, a time when a direct handover of the child to the parent or carer is required. The researcher and teacher/teaching assistant handed out information sheets directly to parents. This helped to associate the researcher with the school and with the class teacher, which it was hoped would build trust, and meant that the researcher was available for parents to ask any questions about the research. The researcher did not approach parents, except to give them the information sheet, to avoid parents feeling harassed to take part. This recruitment was conducted after the first child dental examination to establish trial eligibility had been carried out, so there was no possibility that this approach could be identified with trial recruitment, which had finished by this point. The information sheet made it clear that the trial recruitment had finished and that the current recruitment was for a research interview only, to find out why some parents decided not to take part in dental studies and programmes to inform future interventions. Information sheets were given only to parents who had not returned any paperwork to the trial. Parents were told that the researcher would be in the school (accessible via the school reception desk) one day during the following week, when parents could drop in to do an interview if they wanted. The interviews were set up on a 'drop-in' basis to make it easy and flexible for parents, rather than arranging an appointment time, and to further avoid parents feeling harassed to take part in the research. Year 2 class teachers were asked to remind parents about the interviews the day before. The information sheet also included the researcher's telephone number in case parents had any queries about the interviews.

This recruitment was carried out in years 1 and 2 of the study (for cohorts 1 and 2), and for cohort 2 an incentive of a £10 shopping voucher was offered for a completed interview.

Parents who withdrew their children from the trial were also sent a letter inviting them for a telephone interview about their reasons for deciding to no longer take part. The target for the study was to recruit up to 20 withdrawing parents and to compare data by trial arm.

The results of these recruitment efforts and the data collected on reasons for non-participation are discussed in detail in *Findings*.

Data analysis

Treatment acceptability as measured by observed signs of distress

A 'signs of distress' scale independently measured by both the dental nurse and dental hygienist was calculated as the mean of the valid item responses (scored 1 for yes and 0 for no; see *Appendix 16*). When three or more of the items were missing, the score was set as 'missing'.

Treatment acceptability as determined using the Delighted–Terrible Faces scale

Child-rated treatment acceptability at each treatment visit used the DTF scale. Faces were scored 1–5 (happy to sad) and a mean score calculated over the five items. The distribution of this score precluded linear regression analysis and the results were categorised into a binary outcome as follows (scores 1–2.49 as 'happy' and scores 2.5–5 as 'sad'). When three or more of the items were missing, the DTF score was set as missing.

The determination of acceptability between intervention arms of the trial is reported as unadjusted and adjusted ORs, calculated as described in *Chapter 2*.

Qualitative data

All interviews were digitally recorded and fully transcribed. Transcriptions were then uploaded to NVivo version 9 (QSR International, Warrington, UK) and analysis was conducted in three stages. First, data were analysed by means of framework analysis, using NVivo version 9 software.⁶⁵ Framework analysis is a method that organises responses by respondent and interview content, and allows analysis by case or theme so that they can be compared easily.⁶⁵ The research questions and interview schedule questions formed the initial categories for the framework; any additional categories for other themes that emerged from the data were added to the framework. For example, children tended to discuss not only the FS or FV treatment itself, but also the chair, protective glasses, air/water sprays and so on, and so these were recorded as separate factors affecting acceptability. Separate frameworks were produced for each trial arm, interviewee group (child, parent, CDS staff, school staff), time point (first, second and third year of trial) and school deprivation level (high/low). This was to facilitate reporting by each interviewee group and comparison between trial arms, deprivation level and across time. Most of the categories in each framework were similar (e.g. all interviewees were asked about treatment acceptability), but a few varied (e.g. only the CDS staff framework had a thematic category for child co-operation). Each category in each of the frameworks was summarised in a short list of bullet points in summary tables; this enabled a summary of each theme to be produced, but also contained sufficient detail about variance between responses to avoid bias in the reporting.

The qualitative data analysis took a postpositivist approach (compared with the constructivist paradigm that is often adopted in qualitative research). This was primarily because the research questions for the process evaluation were very specific to particular aspects of the treatment and setting, rather than being an exploratory or in-depth study of behaviours. Furthermore, the child and parent interviews were relatively short, and answers tended to be brief and to the point. The children were too young to provide very elaborate answers and parents were often very busy (young children or infants were frequently heard in the background of telephone interviews). The data collected therefore matched all interview schedule categories very closely and did not elaborate beyond brief facts or opinions. This made a framework analysis

appropriate for analysing this type of data, rather than the multilevel interpretive coding that would be appropriate for more in-depth data. For the same reason, only one researcher (SMT) analysed the data. Reflexivity in terms of the interview schedule or interpretation of the data was also not conducted, as the interpretative nature of data analysis is not emphasised in postpositivist research. However, potential influences on the data were noted when appropriate (e.g. a probable social desirability bias in reporting oral hygiene and dietary behaviours, as noted in *Impact of treatment and trial on oral health behaviour*).

In the second stage of analysis, the framework summaries were compared by trial arm, deprivation level and time points (years 1 and 3 of the trial).

Findings

Overall acceptability of FS/FV treatment in a school setting was high for children, CDS staff, school staff and parents. Factors influencing acceptability were largely non-FS/non-FV aspects of treatment or aspects of the wider treatment or school setting. These are discussed separately in the following sections. First, the acceptability is described as it was observed during treatment and reported by the children immediately post treatment. Next, the acceptability of the actual FS/FV treatments for children is reported, before global acceptability for children is reported, which often depended on wider aspects of the dental treatment. The section after this describes the acceptability of the treatment setting to children, parents, CDS staff and schools. Finally, the impact of the SoV trial on oral hygiene behaviour and the reasons for participation and non-participation in SoV are discussed.

Acceptability of treatment

Signs of distress

Immediately after treatment in the MDC, the dental hygienist and the dental nurse recorded signs of adverse behaviour during FS or FV placement. Observations during the baseline examination are reported in *Tables 69* and *70*. The equivalent data at the 30-month treatment visit are shown in *Tables 71* and *72*.

Overall, the proportion of children displaying adverse behaviours or showing signs of distress during treatment at baseline, as observed by the dental hygienist, was small: 97 of the 468 children in the sealant treatment arm and 40 out of 464 children in the FV arm of the study. Children in the FS arm were more likely to gag and to cry. There was good agreement between the observations made by the dental hygienist and the accompanying dental nurse, although the nurses were more likely to observe and report excess movement of arms and legs during treatment.

TABLE 69 Dental hygienist observation of behaviour during baseline treatment, by trial arm

Behaviour	Intervention arm		Total (N = 932), n (%)
	FS (N = 468), n (%)	FV (N = 464), n (%)	
Vomiting	4 (0.9)	3 (0.7)	7 (0.8)
Gagging	39 (8.4)	16 (3.5)	55 (6.0)
Crying	16 (3.5)	3 (0.7)	19 (2.1)
Excessive arm movements	22 (4.8)	8 (1.7)	30 (3.3)
Excessive leg movements	2 (0.4)	5 (1.1)	7 (0.8)
Other signs of distress	67 (14.6)	20 (4.4)	87 (9.5)

TABLE 70 Dental nurse observation of behaviour during baseline treatment, by trial arm

Behaviour	Intervention arm		Total (N = 931), n (%)
	FS (N = 467), n (%)	FV (N = 464), n (%)	
Vomiting	2 (0.4)	1 (0.2)	3 (0.3)
Gagging	35 (7.6)	13 (2.8)	48 (5.2)
Crying	17 (3.7)	4 (0.9)	21 (2.3)
Excessive arm movements	24 (5.2)	12 (2.6)	36 (3.9)
Excessive leg movements	12 (2.6)	3 (0.7)	15 (1.6)
Other signs of distress	52 (11.4)	20 (4.4)	72 (7.9)

TABLE 71 Dental hygienist observation of behaviour during 30-month treatment, by trial arm

Behaviour	Intervention arm		Total, n (%)
	FS, n (%)	FV, n (%)	
Vomiting	0 (0)	0 (0)	0 (0)
Gagging	6 (1.4)	7 (1.7)	13 (1.5)
Crying	3 (0.7)	2 (0.5)	5 (0.6)
Excessive arm movements	0 (0)	2 (0.5)	2 (0.2)
Excessive leg movements	0 (0)	0 (0)	0 (0)
Other signs of distress	7 (1.7)	12 (2.9)	19 (2.3)

TABLE 72 Dental nurse observation of behaviour during 30-month treatment, by trial arm

Behaviour	Intervention arm		Total, n (%)
	FS, n (%)	FV, n (%)	
Vomiting	0 (0)	1 (0.2)	1 (0.1)
Gagging	4 (1.0)	10 (2.4)	14 (1.7)
Crying	3 (0.7)	3 (0.7)	6 (0.7)
Excessive arm movements	1 (0.2)	1 (0.2)	2 (0.2)
Excessive leg movements	0 (0)	0 (0)	0 (0)
Other signs of distress	8 (1.9)	14 (3.3)	22 (2.6)

To facilitate analysis, the adverse outcomes over the course of the trial as observed by the dental hygienist and the dental nurse were dichotomised (any adverse outcome vs. no adverse outcomes recorded) for analysis (Tables 73 and 74). The behaviours observed differed across the intervention arms of the study. At baseline, 21% of participants displayed some form of adverse behaviour, but this fell steadily at subsequent treatment visits up to the final treatment visit at 30 months, at which only 2.6% of the participants were observed to have some form of adverse behaviour during treatment. In contrast, the proportion of children showing signs of adverse behaviour during the application of FV remained more constant in the course of the trial, ranging from 8.7% at baseline to 3.8% and 4.1% at the 24- and 30-month visits, respectively. During the trial, increased familiarity with the treatment process and increased ability to cope as the children got older are probable influences on these findings.

TABLE 73 Trends in signs of distress as observed by the dental hygienists at baseline and at 6, 12, 18, 24 and 30 months

Time point	Intervention arm		Overall, n (%)
	FS, n (%)	FV, n (%)	
Dichotomised hygienist-rated adverse outcome scale (yes)			
Baseline	97 (21.0)	40 (8.7)	137 (14.9)
6 months	72 (15.4)	35 (7.9)	107 (11.7)
12 months	40 (8.7)	24 (5.3)	64 (7.0)
18 months	20 (4.4)	23 (5.2)	43 (4.8)
24 months	18 (4.1)	16 (3.8)	34 (3.9)
30 months	11 (2.6)	17 (4.1)	28 (3.3)

TABLE 74 Trends in signs of distress as observed by the dental nurse at baseline and at 6, 12, 18, 24 and 30 months

Time point	Intervention arm		Overall, n (%)
	FS, n (%)	FV, n (%)	
Dichotomised nurse-rated adverse outcome scale (yes)			
Baseline	92 (20.0)	36 (7.8)	128 (13.9)
6 months	56 (12.0)	32 (7.2)	88 (9.7)
12 months	23 (5.0)	24 (5.3)	47 (5.2)
18 months	16 (3.5)	26 (5.9)	42 (4.7)
24 months	15 (3.4)	15 (3.6)	30 (3.5)
30 months	14 (3.3)	25 (5.9)	39 (4.6)

The difference between trial arms at baseline as observed by the dental hygienists at the baseline examination was subject to two-level and single-level logistic regression (*Tables 75 and 76*).

Model 1 is a two-level logistic model of child within school, whereas model 2 is a single child-level model for the dichotomised adverse outcome scale. It can be seen that the addition of school as a level does not alter the main conclusion that a significantly higher proportion of children in the FS arm experienced adverse outcomes at baseline. Both models adjust for the balancing variables from the randomisation (sex and baseline caries).

A similar analysis was of the behaviours observed by the treating dental hygienist conducted at the 30-month treatment visit (*Table 77*). Slightly more adverse events were recorded in the FV arm at 30 months, although the number of events was low in both intervention arms.

TABLE 75 Summary data for the dichotomised hygienist-rated adverse outcome scale at baseline

Adverse outcome	Intervention arm		Overall, n (%)
	FS, n (%)	FV, n (%)	
No	365 (79.0)	420 (91.3)	785 (85.1)
Yes	97 (21.0)	40 (8.7)	137 (14.9)

TABLE 76 Two-level and single-level logistic regression of the dichotomised hygienist-rated adverse outcome scale at baseline

Model	OR ^a	95% CI	p-value	ICC
Model 1	0.337	0.22 to 0.51	< 0.001	0.152
Model 2	0.357	0.24 to 0.53	< 0.001	n/a

n/a, not applicable.
a FV compared with FS. Analysis adjusted for baseline caries prevalence and sex.

TABLE 77 Summary data for the dichotomised hygienist-rated adverse outcome scale at 30 months

Adverse outcome	Intervention arm		Overall, n (%)
	FS, n (%)	FV, n (%)	
No	411 (97.4)	401 (95.9)	412 (96.7)
Yes	11 (2.6)	17 (4.1)	28 (3.3)

Again, model 1 is a two-level logistic model of child within school, whereas model 2 is a single child-level model for the dichotomised adverse outcome scale. It can be seen that the addition of school as a level did not alter the main conclusion that the proportion of children experiencing adverse outcomes at 30 months was slightly higher in the FV arm than in the FS arm, but the difference was not significant (*Table 78*). Both models adjust for the balancing variables from the randomisation (sex and baseline caries).

Acceptability of fissure sealant/fluoride varnish treatment for children

Participants' perception of treatment acceptability

Treatment acceptability was assessed from the child's perspective through a DTF scale (see *Appendix 12*), completed by all children in the MDC immediately following the initial application of FS/FV and at each follow-up visit. The scores recorded at the baseline treatment visit are recorded in *Table 79*. It is apparent that time and taste were the dominant factors influencing acceptability. To facilitate analysis of the trends observed over the course of the trial, the data were dichotomised to most happy/happy versus neither happy nor sad/sad/most sad.

The proportion of children who opted for the neither happy nor sad face, the sad face or the very sad face at baseline to describe their feelings on completion of treatment was much higher in the FS group than in the FV group (49.2% vs. 27.1%). This proportion reduced during the course of the study so that by the

TABLE 78 Two-level and single-level logistic regression of the dichotomised hygienist-rated adverse outcome scale at 30 months

Model	OR ^a	95% CI	p-value	ICC
Model 1	1.63	0.75 to 3.55	0.221	0.087
Model 2	1.59	0.74 to 3.45	0.238	n/a

n/a, not applicable.
a FV compared with FS. Analysis adjusted for baseline caries prevalence and sex.

TABLE 79 Delighted–Terrible Faces scale scores at baseline treatment visit

Score	Intervention arm		Total (N = 926), n (%)
	FS (N = 463), n (%)	FV (N = 463), n (%)	
How did you feel during the treatment?			
1 – most happy	245 (53.1)	319 (69.0)	564 (61.1)
2	97 (21.0)	56 (12.1)	153 (16.6)
3	77 (16.7)	59 (12.8)	136 (14.7)
4	22 (4.8)	22 (4.8)	44 (4.8)
5 – most sad	20 (4.3)	6 (1.3)	26 (2.8)
If you had to have the treatment tomorrow how would you feel?			
1 – most happy	180 (39.1)	212 (46.0)	392 (42.6)
2	104 (22.4)	116 (25.2)	217 (23.6)
3	85 (18.5)	62 (13.4)	147 (16.0)
4	43 (9.3)	43 (9.3)	86 (9.3)
5 – most sad	51 (11.1)	28 (6.1)	79 (8.6)
How do you feel about the time it took to have the treatment?			
1 – most happy	161 (35.4)	273 (59.2)	434 (47.4)
2	65 (14.3)	86 (18.7)	151 (16.5)
3	95 (20.9)	56 (12.1)	151 (16.5)
4	64 (14.1)	24 (5.2)	88 (9.6)
5 – most sad	70 (15.4)	22 (4.8)	92 (10.0)
How did you feel about the taste of the treatment?			
1 – most happy	75 (16.5)	184 (39.8)	259 (28.3)
2	39 (8.6)	48 (10.4)	87 (9.5)
3	47 (10.4)	53 (11.5)	100 (10.9)
4	116 (25.6)	78 (16.9)	194 (21.2)
5 – most sad	177 (39.0)	99 (21.4)	276 (30.1)
Did the treatment make you feel like you wanted to be sick?			
1 – most happy	280 (61.5)	299 (64.7)	579 (63.1)
2	22 (4.8)	26 (5.6)	48 (5.2)
3	35 (7.7)	43 (9.3)	78 (8.5)
4	53 (11.6)	42 (9.1)	95 (10.4)
5 – most sad	65 (14.3)	52 (11.3)	117 (12.8)

30-month examination, only 16.8% of the FS-treated group reported that they were neutral or sad immediately following treatment. This contrasts with the findings in the FV arm, in which there was a gradual increase in the proportion of children opting for the neutral or sad options on the DTF scale between baseline and 30 months (*Table 80*).

Two-level and single-level logistic regression models were constructed to determine the difference between intervention arms at baseline and at 30 months (*Tables 81–84*).

TABLE 80 The number of participants selecting 'neither happy nor sad, sad or very sad' at each of the time points in the clinical trial by intervention arm

Time point	Intervention arm		Overall, <i>n</i> (%)
	FS, <i>n</i> (%)	FV, <i>n</i> (%)	
Dichotomised modified DTF scale ('neither happy nor sad, sad or very sad')			
Baseline	224 (49.2)	125 (27.1)	349 (38.1)
6 months	131 (28.7)	134 (30.1)	265 (29.4)
12 months	92 (21.2)	148 (32.7)	240 (27.1)
18 months	77 (17.1)	140 (31.9)	217 (24.4)
24 months	81 (18.7)	159 (37.9)	240 (28.1)
30 months	71 (16.8)	171 (40.7)	242 (28.7)

TABLE 81 Summary data for the dichotomised modified DTF scale at baseline

	Intervention arm		Overall, <i>n</i> (%)
	FS, <i>n</i> (%)	FV, <i>n</i> (%)	
Very happy or happy	231 (50.8)	337 (72.9)	568 (61.9)
Neither happy nor sad, sad or very sad	224 (49.2)	125 (27.1)	349 (38.1)

TABLE 82 Two-level and single-level logistic regression of the dichotomised modified DTF scale at baseline

Model	OR ^a	95% CI	<i>p</i> -value	ICC
Model 1	0.38	0.29 to 0.50	< 0.001	0.012
Model 2	0.38	0.29 to 0.50	< 0.001	n/a

n/a, not applicable.

a FV compared with FS. Analysis adjusted for baseline caries prevalence and sex.

TABLE 83 Summary data for the dichotomised modified DTF scale at 30 months

	Intervention arm		Overall, <i>n</i> (%)
	FS, <i>n</i> (%)	FV, <i>n</i> (%)	
Very happy or happy	351 (83.2)	249 (59.3)	600 (71.3)
Neither happy nor sad, sad or very sad	71 (16.8)	171 (40.7)	242 (28.7)

TABLE 84 Two-level and single-level logistic regression of the dichotomised modified DTF scale at 30 months

Model	OR ^a	95% CI	<i>p</i> -value	ICC
Model 1	3.63	2.60 to 5.07	< 0.001	0.073
Model 2	3.44	2.19 to 4.75	< 0.001	n/a

n/a, not applicable.

a FV compared with FS. Analysis adjusted for baseline caries prevalence and sex.

Model 1 is a two-level logistic model of child within school, whereas model 2 is a single child-level model for the DTF scale. It can be seen that the addition of school as a level does not alter the main conclusion that the proportion of children reporting that they were happy or very happy at baseline was significantly higher in the FV arm than in the FS arm, and that the proportion of children reporting that they were happy or very happy at 30 months was significantly higher in the FS arm than in the FV arm. Both models adjust for the balancing variables from the randomisation (sex and baseline caries).

From the above, it is obvious that the acceptability of the technologies under test as judged by the children immediately post treatment was different at different time points in the trial. There are two main issues:

1. At baseline, the children in the FV arm were significantly happier than those in the FS arm, this situation being reversed at the final treatment at 30 months.
2. Those receiving FS became happier as the trial progressed; however, in contrast, in the FV arm there was a modest decrease in the number of children who chose a happy face over the course of the trial.

These findings are in line with what might be expected from a clinical perspective. As the FSs were applied at the beginning of the study as soon as the FPMs erupted, the treatment was more invasive and intense and, as described in *Chapter 3*, took longer. The children receiving FV, however, had to experience treatment of approximately the same intensity throughout the study.

Qualitative findings on treatment acceptability

In addition to the quantitative determination of treatment acceptability, treatment acceptability formed a major component of the qualitative investigations. In the interviews, the children largely talked about the actual FV or FS treatment in terms of taste. FV was variously described as 'banana jam/gel/paste', tasting like 'candy floss', 'oranges' or 'apple', being 'burny' and tasting 'a bit funny and a bit nice'. FS was described as tasting like water, tasting like 'sour apples' and being 'very horrible' or 'disgusting' (although some children liked the taste). Children in year 1 of the study tended to think of the treatment as a 'banana gel/paste' and, as children were not always aware that there were two different treatments, children in both arms talked about a banana flavour. Because CDS staff were aware that not all children liked banana flavour and that this might make them reluctant to co-operate with further treatment, they referred to a 'fruity taste' when talking to children. In the final year interviews, children discussed different fruit flavours of the treatment, and some children thought that different flavoured treatments were used or wanted to receive a different flavoured 'gel' on each visit.

Children's opinions were mixed in terms of whether or not they liked the taste; some had mild like/dislike, whereas others had stronger positive or negative reactions:

Interviewer: All right, so you both don't like the taste of it? Is it just a little bit disgusting or is it really awful?

Child 1: Really awful.

Child 2: It's really awful.

Paired child interview, one FS arm and one FV arm, year 3

Interviewer: And what do you think about having a dental van coming to the school?

Child 1: I like it, I feel happy I do.

Child 2: I feel happy too.

Interviewer: And why do you like it and why do you feel happy?

Child 1: Because when like you have this banana stuff.

Child 2: Aw yeah, it tastes really nice.

Child 1: It tastes nice.

Interviewer: Is that what you like about it?

Child 1: Yeah.

Paired child interview, FV arm, year 3

I think the banana gel is a bit bleurgh.

Paired child interview, FV arm, year 3

It's not the best taste but it's not the worst taste.

Paired child interview, FS arm, year 3

Many children said that their experience of the treatment and of visiting the MDC was good, and said they felt 'OK' or 'fine' about it, even if they did not like the taste:

Interviewer: So can you tell me what you thought about going to the dentist when you went?

Child 1: It was quite fun.

Child 2: It was quite fun and it tasted disgusting.

Interviewer: OK [to child 2] you thought it was disgusting and [to child 1] you thought it was quite fun.

Child 1: I thought it was fun.

Child 2: It was fine but it tasted horrible.

Paired child interview, FS arm, year 1

Several clinical staff members thought that children did not always complete the DTF form in a way that was internally consistent or consistent with what they expressed to staff during their treatment visit; this may be because of the number of different factors driving acceptability for children, as reflected in the previous quotation.

In year 1 of the study, in the FS arm, 13 of the 16 children who made clear statements about the taste of treatment made negative comments about the taste, whereas in the FV arm children's reactions to the taste were more evenly spread. However, children in the FV arm who did not like the taste were more likely to express negative feelings about having to have more treatment in the future, and half of these children said nothing positive about the treatment experience at all. This may indicate that, although children were less likely to dislike the FV, those who did dislike it had stronger reactions to the taste of the treatment than did children in the FS arm. However, these results should be interpreted with caution, as the sample sizes were small.

In year 3 of the study, there were far fewer very negative comments about having more treatment than there had been in year 1. Children in the FV arm again made a fairly even spread of comments about the taste, from positive to negative, whereas FS children were more likely to make 'middling' assessments.

This may be because some FS arm children would not have been having further treatment at this stage, unless the sealant needed to be reapplied. Two of the FS children thought that the process was quick, and two others in this group mentioned the treatment visits not always being the same. Of the children who made negative comments in the FV arm, all mentioned the taste and/or feeling sick, although only one said that they would be nervous about going back for more treatment because of this. There were no differences by deprivation level.

In the final year of the study, no child interviewed reported very negative overall attitudes towards having treatment, even though some children still reported not liking the taste. For example, one FS child in year 3 said that they would be excited to go for treatment again, but also said that the taste was really awful. Overall, most children were generally tolerant about having FS/FV treatment by this stage:

Interviewer: When you have to go and have your treatment in the dental van, what do you think about that?

Child 1: It was all right but the taste was a little bit not that nice.

Interviewer: Not that nice.

Child 1: It tasted like bananas.

Interviewer: So you didn't really like the taste but apart from that, it was all right you said?

Child 1: Yeah.

Interviewer: It was OK. And what about you [to child 2]? What do you think?

Child 2: The taste was not that nice and it tasted like oranges.

Interviewer: It tasted like oranges. OK. So not that nice but apart from the taste, how was it having to go and have the treatment?

Child 2: Not that bad.

Paired child interview, FV arm, year 3

The qualitative data on treatment acceptability are similar to the findings from the DTF scales and co-operation scales, in that the acceptability of FS treatment was low overall in year 1 but increased over time.

Other aspects of treatment were mentioned with less frequency than taste. Children very rarely commented on the length of treatment unless they were prompted and seemed unconcerned by this aspect of treatment. Perceptions of length of treatment depended more on the individual child than on the trial arm. Children were more likely to comment on the time taken in terms of not liking to wait in dentist waiting rooms (which they reported happened more commonly in community dentist offices than in the MDC as part of the SoV trial). A very small number of children mentioned the texture of their teeth afterwards as being sticky (FV) or 'bumpy/dotty' (FS). A few children mentioned feeling sick or vomiting: one child in the FV arm and two in the FS arm mentioned feeling or being sick in year 1 and two children in the FV arm in year 3 mentioned feeling sick. Most children did not notice discoloration, and the few who did were not concerned by this. When asked whether or not their teeth had changed after treatment, some children thought that the treatment had made their teeth stronger, whiter, cleaner or 'fresh'. When children commented on changes in their teeth, this tended to be in relation to normal changes such as their adult teeth appearing, rather than any changes attributable to FS/FV.

Parental reports of treatment acceptability

Parent accounts of child acceptability corroborated child reports. Parents said that children found it novel and exciting to visit the MDC (known colloquially as 'the van') and that they liked various aspects of treatment such as being with their friends and being given stickers:

Interviewer: Has he ever said anything about the taste or about how long it takes or anything like that?

Parent: He said it's banana taste.

Interviewer: Does he like that or does he not like that?

Parent: He likes that.

Interviewer: He likes the taste, OK. And does he say anything else about the van or going with his friends or anything like that?

Parent: He just says he likes going on the van and having a sticker.

Interviewer: And he likes the sticker, do you know what he likes about going on the van?

Parent: I think it's the chair, because they let him play with the chair.

Parent interview, FS arm, year 3

Many parents said that their children did not say much about the treatment but would have complained if they had found the treatment very objectionable. A small number of children had reported to their parents that they did not like the taste or another aspect of treatment (e.g. that it was 'gluey') but, again, acceptability was often based on more than one factor:

Parent: She said that it tasted horrible.

Interviewer: OK.

Parent: That was it really just it didn't taste very nice but she was delighted because she had stickers [laughs] you know I was like 'What was it like, what did they do?' and she said 'They put something in my mouth and it didn't taste very nice'.

Parent interview, FS arm, year 1

In year 1, children either did not say anything about the treatment to their parents or said that it tasted funny or that they did not like the taste. In year 3, children still either said little or reported that they did not like the treatment, but children at this stage also mentioned to parents aspects of the treatment that they liked. There were no differences between trial arms or by deprivation level.

Parents in the high-deprivation schools in the first year of the study were most likely to report discoloration of teeth from the treatment, in both trial arms. In the final year of the study, a very small number ($n = 3$) of parents in the FV arm reported discoloration. If parents did notice discoloration, they were not always sure that this was because of the treatment; other explanations were that it might be because of their child's age or inadequate brushing. No parent was concerned about discoloration, and perceptions did not differ by trial arm.

A few parents thought that their child's teeth were whiter or shinier; some were not sure about changes but expressed a hope that the child's teeth were stronger or more protected because of the treatment received.

School staff reports of treatment acceptability

Staff reported that the MDC and CDS service was well liked in schools by children; one head teacher commented that usually children were disappointed if they were not called to attend. One school staff member commented that if children did not like an aspect of treatment they forgot about it soon after returning to the classroom.

Community Dental Service staff reports of treatment acceptability

Throughout the study, CDS staff had mixed opinions about which treatment was more acceptable to children. They observed varied reactions to the treatment and different aspects of treatment that were more or less popular:

The children react differently to be honest. Some of them love the varnish or some of them hate the varnish, some of them play up because their friends are there or whatever, they have a different reaction and then some of them are good with the sealants as well.

CDS staff interview, year 2

Community Dental Service staff commented that children were generally tolerant and well behaved, regardless of whether they liked the treatment.

In year 1, more staff thought that FV was better liked by children because it was quicker and did not involve cotton wool rolls, and because some children did not like the taste of the FS fixer. In year 2, the staff commented in more detail about the pros and cons of both treatments: FV was quicker and easier to apply, but it was also sticky, could cause nausea and had a lingering taste, whereas children could rinse after FS treatment; if children gagged easily it meant that applying FS could be difficult, and children sometimes found it difficult to keep their mouth open for a long time, but FS usually required only check-ups rather than reapplication. They also mentioned that FV was easier than FS for a difficult child as it was the quicker treatment. Staff used various tactics to encourage children, such as bringing nervous children back later in the day to retry treatment, treating a nervous child first (so that the child did not have to wait) or last (so that the child could observe other children receiving treatment), and sitting a child further upright to reduce gagging.

Staff in years 2 and 3 also said that children were very accepting of treatment and that refusals were rare, but they did note that acceptability still varied and that some children liked the treatment or taste and some did not. By this point, some children remembered not liking the treatment and could react negatively when attending again, which could then affect the other children they were with. One staff member thought that children from more deprived areas reacted more negatively when coming back for treatment. However, some FS children were disappointed that they did not receive any treatment when other children did.

Various CDS staff comments mirrored what children reported. One staff member commented that children receiving FS disliked the cotton wool rolls more than they disliked the length of treatment. A number of staff members reported that whether or not children found the treatment acceptable was largely driven by taste, and also that some children thought the treatment was too quick and would have liked more time out of the classroom. Staff also commented that children liked different aspects of treatment, particularly laughing at each other wearing the protective glasses; preferring to be with their friends and being less nervous if they were accompanied; and enjoying the novelty and excitement of being on the MDC:

Oh they love coming on the van. They love it. They always ask who drives it and where do people, some, some think that they sleep there overnight and it turns into a caravan but they love it, they love coming on. What's this drawer for, you know, yeah, they love coming on.

CDS staff interview, year 2

The CDS staff members' comments that children were chattier and asked more questions in year 3 of the study also corroborated some children's reports that they felt more confident now that they were older.

Global intervention acceptability for children

Turning to the information analysed from the interviews with the participating children, the primary finding on the overall acceptability of FS/FV treatment for children was that there were many factors that contributed to whether or not children found the treatment acceptable. Most of these factors were related not to the FS/FV aspects of the MDC visit but rather to more general aspects of treatment or to the context in which the treatment was delivered.

Most children commented that 'going to the van' was 'fun', 'brilliant' and 'good' and that it was exciting to go there (the 'van' is the term children used to describe the MDC). Receiving stickers was a very popular aspect of MDC visit, and three children mentioned that they liked the CDS staff. When comparing a visit to the MDC with a visit to a family/community dentist, most children also expressed their views in relation to factors beyond the actual treatment received, such as being given stickers, the speed of the visit, which visit was warmer and the van being fun. Some children also mentioned that they liked having their teeth looked after or protected:

I like the dentist because they look after your teeth and keep them clean.

Child interview, FV arm, year 1

Fourteen children in year 1 of the study mentioned feeling scared or nervous about the treatment; of these, 12 said that being with friends (children normally attended the MDC in groups of three) made them less nervous or feel safer. In year 3 of the study, fewer children mentioned feeling nervous, and in the low-deprivation schools four children commented that they felt more confident about being at the dentist now that they were older and more used to the treatment visits:

Child 1: We did both say we were nervous when we went, when we were.

Child 2: Yeah, when we were younger, 'cos it was our first time.

Child 1: Yeah 'cos it was less.

Child 2: We were like . . . not confident.

Child 1: Yeah.

Child 2: 'Cos we were just too young to go on our own, not like on our own like.

Interviewer: You were quite young when you started though.

Child 2: Yeah, I was talking about before.

Child 1: Because you're like quite scared, because you haven't been to the dentist oftenly[sic].

Child 2: Then you might need . . .

Child 1: So when you get older and older and . . .

Child 2: You'll be more confident.

Child 1: Yeah.

Paired child interview, one FS arm and one FV arm, year 3

Although the older children generally felt more relaxed and confident about a visit to the MDC, they were also more aware of what was going on around them. In year 3 of the study, a small number of children reported that the examination made them feel anxious because they did not understand the tooth-numbering terminology the CDS hygienist used and were worried that there might be something wrong with their teeth:

Child 1: They say stuff like numbers and stuff and we don't really know what that means.

Interviewer: You don't know what that means, OK.

Child 1: So like, they could be saying that our teeth are really bad or really good but we don't know.

Child 2: Like A2 and A3 and that.

Child 1: Yeah.

Interviewer: Yeah.

Child 2: AC.

Interviewer: Sounds funny doesn't it?

Child 2: Yeah.

Child 1: Yeah.

Interviewer: So would you like to know more, you'd like to understand what they're saying?

Child 1: Yeah.

Paired child interview, one FS arm and one FV arm, year 3

Children also frequently mentioned generic aspects of the dental treatment they liked, particularly the moving dental chair and protective (and often coloured) glasses. Feelings about the three-in-one syringe were mixed, as some children found it unpleasant but some liked it because it was 'ticklish'. The cotton wool rolls were the least popular aspect of treatment and a few children expressed a dislike of having their teeth 'scraped'/'poked'. There were no differences in preferences between the FS and FV trial arms. Children's responses to what they thought about the overall treatment often centred on these wider factors rather than on the FS/FV itself:

Interviewer: So can you tell me, what did you think about going to the dentist earlier this week?

Child 1: It was good, I liked it.

Interviewer: It was good . . .

Child 2: It was fun.

Interviewer: And you thought it was fun [to child 2], OK. And what did you like about it? [Pause.] Or are you not sure?

Child 1: Because you got to sit on the special chair.

Interviewer: The special chair, a magic chair?

Child 1: Yeah.

Interviewer: *What was special about it? Why was it a good chair?*

Child 2: *Because it can move.*

Interviewer: *Is that fun?*

Child 1: *Yeah, and I like the glasses.*

Interviewer: *What do you like about the glasses?*

Child 1: *Because they protect our eyes and face.*

Interviewer: *They protect your eyes. Are they a special colour?*

Child 2: *White.*

Interviewer: *White?*

Child 2: *Yeah.*

Interviewer: *OK. Is there anything else that you liked about going?*

Child 1: *Yeah, I was excited.*

Interviewer: *You were excited . . .*

Child 1: *And because you got to go in the van.*

Interviewer: *Oh right, what do you like about the van?*

Child 1: *Because um [pause] can't remember.*

Interviewer: *You're not sure, that's OK. But it's fun going in the van?*

Child 1: *Yeah.*

Paired child interview, FV arm, year 1

Taste was the main aspect of the actual treatment acceptability mentioned by children, but it was one of several factors:

Interviewer: *If somebody said you've got to go and have that same treatment done again tomorrow, how would you feel about that?*

Child 1: *I wouldn't mind.*

Interviewer: *You wouldn't mind [to child 1] and how about you [to child 2]?*

Child 2: *It would be OK.*

Interviewer: *It would be OK. So it wouldn't be fantastic but it would be OK?*

Child 1: *It would be fantastic.*

Interviewer: *Why would it be fantastic?*

Child 1: *Because I love the banana gel.*

Interviewer: *Is that the best thing about going?*

Child 1: *No.*

Interviewer: *What's the best thing about going?*

Child 1: *Getting the sticker.*

Paired child interview, FV arm, year 3

A small number of children were so enthusiastic about the treatment visits that they responded (unprompted) that they would be happy to have the treatment done all day/every day:

Interviewer: *If the van came back tomorrow and you had to have it done all over again, how would you feel about that?*

Child: *It don't matter, I'll have it every day.*

Interviewer: *OK. Why would you have it every day?*

Child: *Because the chair is fun.*

Interviewer: *Is that your favourite thing?*

Child: *Yeah.*

Paired child interview, FV arm, year 1

Children in both trial arms mentioned similar acceptability factors in year 1 and year 3 of the study, such as liking being with their friends, treatment being good for their teeth, and liking the stickers and the moving chair, and mixed attitudes towards different aspects of the treatment, such as the three-in-one syringe:

Interviewer: *And what do you think about going there for the treatment?*

Child 1: *I think it's really good idea.*

Child 2: *Mm hm.*

Interviewer: *And what's good about it?*

Child 1: *It's like, we can get to wear some glasses, we can get a sticker, stuff like that.*

Interviewer: *Mm hm.*

Child 1: *We don't get bad teeth when we're older.*

Paired child interview, FV arm, year 3

In year 3 of the study, children reported that some people in their class liked treatment and some did not. However, most children in year 3 were more likely to report that they were 'fine' or happy/excited to go for treatment, even if they did not like all aspects of it.

Acceptability of treatment setting

Acceptability of treatment setting for children

To elicit information about the acceptability of the FS/FV treatment, children were asked if they preferred being in class or leaving class to visit the dentist at the MDC. In year 1 of the study, most children did not express a clear preference or were indifferent. Children who did express a preference gave various reasons: they thought that it was important to get dental care, they did not like doing schoolwork/they liked missing class, or they liked going to the MDC. One child said that they preferred being in class because they liked their teacher. There were no differences between the FS and FV trial arms.

In the final year of the study, children were more aware of having to catch up on schoolwork if they missed part of a class to visit the MDC, although this was not a major problem, as children mentioned receiving help from their friends or from the teacher to do this. The main reason that children preferred staying in the classroom was avoiding having to catch up on work later. Two children were not sure about their preference; three children said that, if the lesson was mathematics, they would prefer to go to the dentist.

Acceptability of treatment setting for parents

Several parents thought that their children behaved better, made less fuss or were less nervous about seeing a dental clinician in a school environment:

Parent: He will do it in school.

Interviewer: So he's a bit better in school?

Parent: Yeah, as the teachers are there.

Interviewer: The teachers are around?

Parent: Yeah yeah.

Interviewer: And you're not?

Parent: That's right he's a good boy in school see [laughs] it's an awful thing to say but it's true.

Interviewer: Right, so is it just mainly because of the teachers and because it's a school environment that he behaves better?

Parent: He's never naughty in school.

Parent interview, year 1

Parents did not mind their children missing some class time to attend the MDC. Some pointed out that, as the children were young, missing a small amount of time was not significant. A few also pointed out that the children missed less class time going to the MDC than they would if they went to a community dentist. Parents also appreciated not having to escort children to the appointments and commented that this was very convenient for them. A small number commented that the intervention was good for children who would not otherwise see a dental professional.

Acceptability of treatment setting for school staff

In response to the questionnaire in year 1, the majority of schools indicated that hosting SoV in their school had been straightforward, the programme ran smoothly with minimal disruption to the school, the information received was easy to understand and SoV was similar to existing dental programmes running in schools. CDS communication and co-ordination was good and both CDS and schools were flexible

(e.g. in response to each other's timetables). Six also said that it was interesting to be part of a study and two said that they were pleased to offer it to their children. One head teacher mentioned not knowing details of the study, which would have been helpful in explaining the intervention in response to parent queries. One support teacher had had problems with not being aware that the vans were coming and this causing disruption. One class teacher said that some children did not like the taste of the treatment and that staff had to comfort them when the vans arrived the next time. The only other problems were taking time to explain the study to parents (four respondents mentioned this), explaining the study to teachers in the school (two respondents) and finding the time to respond to requests for data (four respondents). Some schools distributed letters for the study, although some also actively reminded parents to return them, by telephoning or texting parents, reminding them in person and by displaying a poster (in one case). Eleven schools agreed that SoV fitted in with other health programmes or initiatives they were involved in; the most common were tooth-brushing programme and the Healthy Schools scheme. Some schools were unsure whether or not SoV had changed dental behaviour, several thought it made children more aware of the importance of looking after their teeth, although another respondent commented that they did various dental programmes so it was hard to know the effect of SoV on behaviour.

Responses in telephone interviews with school staff (mainly school heads) in year 3 were similar to the questionnaire findings. Two school staff mentioned minor disruption to classes when children left to visit the MDC and a small amount of extra paperwork but said that this was not a problem. Overall, visits to the MDC were not perceived as a problem because they were quick and efficient, and schools were very used to their visits:

Very, very minimal impact really. I mean they come in they do their stuff and off they go again.

School staff interview, year 3

The preventative programme was also perceived as meaning that children would miss less school than they would visiting a community dentist for dental problems later on:

Well I'm hoping, from the information that was provided when I took over the class room is that it was going to protect the children's teeth, that there was going to be less cavities, less absences with them disappearing for full days when they have teeth removed and teeth repaired because they're going to be better protected.

School staff interview, year 3

One school head also commented that the service was very child-friendly, and, because of this, the children were not stressed and their visit to the MDC did not disrupt the school day too much.

School staff were positive about having the CDS service in schools and regarded it as fitting in with their promoting health agenda and also helping them engage with families, which was seen as part of their remit:

Interviewer: What do you think about having the dental clinic on the school grounds?

School staff: Oh absolutely fine.

Interviewer: Mm hm.

School staff: Absolutely fine. I think it was nice for the parents to see.

Interviewer: Mm hm. Why is that?

School staff: Well, because I think a lot of them find dentists, doctors, even crossing the threshold of the school quite intimidating.

Interviewer: *Mm hm.*

School staff: *It's made it more accessible for the community.*

School head interview, year 3

School staff thought that SoV, along with other dental programmes, had improved children's awareness of dental health and oral hygiene.

Feasibility and acceptability of treatment setting for Community Dental Unit staff

Community Dental Service staff found the treatment setting unproblematic on the whole, largely because SoV was integrated with the Designed to Smile dental programme for children in South Wales, which already used MDCs to deliver dental treatment to school children and typically ran very smoothly. CDS staff reported that being part of the SoV trial had created extra paperwork and that this took some extra time, especially early in the trial when staff were still getting used to it but that they were generally positive about being part of the trial and reported no significant impact on how treatment was delivered compared with other CDS services. A small number of staff mentioned that they had little time with each child, which could be a disadvantage as chatting to a child could reduce anxiety sometimes.

Minor difficulties noted included parking a MDC in tight spaces or driving one in bad weather, and occasionally school administrators (the main liaison persons for the CDS in schools) complaining about paperwork or not being as helpful as they might be. One SoV staff member commented that because of the various dental programmes running in schools, each with their own paperwork, schools could get confused between them sometimes. However, most school administrators were helpful; for example, one would assist SoV with recruitment if numbers were low and another would text reminders to parents. Overall, CDS staff found schools very helpful and found that they valued CDSs. CDS staff reciprocated, being careful to organise themselves around the school timetable and events to minimise disruption. Two CDS staff members thought that schools in the more deprived areas were particularly welcoming to the MDC.

Community Dental Service staff also mentioned several aspects of the school setting that made treating children easier, including children being more likely to turn up for appointments:

CDS staff: *In the schools we've got a captive audience.*

Interviewer: *Mm.*

CDS staff: *In the clinic we have horrendous, horrendous DNA [did not attend] rates.*

CDS staff member, year 3 of study

The CDS staff were also able to treat larger numbers of children more quickly in a school setting.

Impact of treatment and trial on oral health behaviour

As discussed in *Chapter 3*, none of the potentially confounding covariates affected treatment outcome by trial intervention arm (see *Table 19*). In the qualitative element of the study, children and parents were asked about changes in oral health behaviour as a result of participating in the trial. Both child and parent interviewees tended to describe low and declining levels of child sugar and fizzy drink consumption:

Child: *Well, I know it's really bad for my teeth and that's why I stopped 'cos I don't want like my teeth to rot and stuff.*

Interviewer: *Yes, you stopped what?*

Child: I stopped drinking fizzy drinks and eating sweets . . . I've stopped chocolate and sweet stuff.

Interviewer: And what made you change?

Child: Cos my mum told me to stop it and I never used to listen to her and now everybody is saying it's bad for your teeth.

Interviewer: Mm.

Child: And so I don't eat it any more.

Interview, year 3

Some children also reported starting to use mouthwash or brushing their teeth more frequently. One child commented that they brushed their teeth more 'to make them grow'. A small number of parents also said that they monitored their child's brushing more closely. There were no differences by trial arm (the sample size was very small to make comparisons in any case, as some children found the concept of change over time difficult to grasp). Some parents and children reported improving the child's diet or tooth-brushing habits because of the input from SoV, sometimes just by acting as a reminder to look after the child's teeth. However, there is likely to be a social desirability bias in the data collected, especially as some parents assumed that the researcher was a dental practitioner (several requests were made by parents to inspect children's or parents' teeth during the study; parents were advised to see a dental practitioner).

Reasons for participating or not participating in Seal or Varnish?

Reasons for participation

Most parents were not fully aware of the details of the treatment or study but were participating to generally benefit their children's teeth and to feel that they had done as much as possible to promote their child's dental health:

I'm thinking myself there's every chance now that I've given her the best chance to look after her teeth then and she may not have decay.

Parent interview, year 3

Most made the decision about participation themselves, although some also consulted their spouse or the child as well. A small number checked with their regular dentist first. Some parents were able to recall that it was a protective treatment that was put on teeth, although not all remembered that it was treating only molars or that there were two different treatments being used. Some thought that SoV included dental education. Randomisation to trial arm was not always understood: one parent thought that their child might receive no treatment, and another thought that their child was 'lucky' to be picked for treatment. Few knew how long the study lasted, and many asked about this during research interviews. A few parents had very little understanding or had completely forgotten the details of the study:

Interviewer: Do you understand what the study is about?

Parent: Not really no.

Interviewer: OK, is there anything, if you had to tell a friend about what Seal or Varnish? was what would you say?

Parent: Well to be honest I don't really know a lot about it.

Parent interview, year 1

However, parents trusted the school and several said that they participated partly because of this:

It was with the school I was quite happy because it was recognised through the school.

Parent interview, year 1

I trust the school with everything.

Parent interview, year 1

Several parents also gave accounts of family members' dental histories and experience of FS/FV, either their own or that of the participating child or another of their children, both positive and negative, and gave this as a reason for participation. Some parents liked that the programme would mean that their children would have dental check-ups more regularly (even if they were already having 6-monthly check-ups at a community dentist) because problems would get picked up more quickly.

A small number of parents (both participating and non-participating) also mentioned the value of doing research and were also willing to participate for this reason (although it was not a primary reason).

Reasons for non-participation

Nineteen parents returned a consent form (including in the second trial recruitment package sent home with children) to be interviewed about non-participation. When contacted by telephone, four said that they were taking part in the trial or had signed up, so no interview was attempted. Five did not answer the telephone or the number was wrong, two had a level of English that was too limited for an interview, two said that they were not participating because they were moving house, one was too busy to do an interview because of family illness and one said that they did not want to do an interview and also commented that they did not participate because they already had a dentist in town. On subsequent cross-checking of the 19 consent forms with trial records, it was found that only 8 of the 19 'non-consenter' parents had not given consent. Six had given consent but were ineligible and five were actually in the trial. It is likely that a majority of parents had completed all the forms their child had brought home from school without checking the content of the form thoroughly and did not realise that the consent forms for non-participation interviews were different from the trial forms and completed and returned all the forms they received. CDS staff reported that this was common in parents receiving paperwork about other dental programmes. Hence, the contacts made with parents who returned these forms did not yield any data on reasons for non-participation, except that parents had not always understood the paperwork they received or completed it correctly.

Twelve parents returned the questionnaire about reasons for non-participation (parents could give multiple responses, and so the number of responses is > 12).

The responses indicate positive and negative reasons for non-participation. Some parents did not participate because they just wanted to continue with existing dental care, some were unsure about SoV's benefit or acceptability to the child, and some were unwilling to take part because it was also a research study (*Table 85*).

The questionnaire also asked about dental care and tooth-brushing habits, to determine whether children with poor dental habits were more or less likely to take part in this type of intervention. According to their parents, three children brushed their teeth at least twice a day, four children brushed their teeth once a day and one child did so less frequently than once a day. All parents said that their child visited a dental surgery regularly.

Face-to-face recruitment at the school handover at the end of the day, through distributing an invitation to participate in a research interview, did not work well for the hardest to reach non-participating parents (those who had never responded to any of the study recruitment materials they had received). This recruitment effort was a second measure to try to collect data on why some parents did not participate in the SoV intervention or study. During recruitment for non-participants at handover time at the end of the

TABLE 85 Parents' reasons for not participating in SoV

Response	Frequency of responses
I wanted my child to continue with their current/normal dental treatment at a local dental surgery	7
I did not understand what the study would involve	3
I did not want to be interviewed for the study	3
I wanted my child to continue their normal treatment from the MDC and did not want them to receive anything different	2
My child did not want the treatment and I did not want to make them have it	2
I was afraid my child might lose their place at the local NHS dentist if they went somewhere else for treatment	1
I wasn't confident that the treatment would be good for my child	1
I was worried about what a dental examination might find in my child's teeth	1
I do not like the school being involved in or knowing too much about my child's health care	1
I do not like taking part in research	1
I did not like being unable to choose which treatment my child received in the study	1
I did not want to have to fill out questionnaires for the study	1
Other: 'My child don't like the fact that he is not able to rinse his mouth after brushing in class, even though I know its fine, but he does not like it. Funny really.'	

school day, no parents queried the researcher, although one or two made more general queries about dental services available in relation to specific problems that their child was having. These parents were given the telephone number for the CDS for information about appropriate dental services.

Five parents across three schools gave consent to be interviewed. One decided not to participate in SoV because they were moving house but would have liked to otherwise and had attended the interview primarily to find out about their own dental treatment. One was participating in the trial and two thought that they had returned consent forms. One of these parents was familiar with FS because their child's older sibling had had this treatment, and they thought that they had consented and so did not know why they were not taking part. Three did not remember receiving any information about SoV but were generally positive about school dental programmes. Two commented that they thought that their child had probably lost the letter sent out from the school and that this had happened with school letters before: 'sometimes she makes paper aeroplanes out of it'. None expressed any negative feelings about taking part in a trial. Therefore, this set of interviews yielded no data on reasons for non-participation, as parents were generally positive about the dental programme, except that, again, that there was confusion about or difficulties with completing the paperwork. This recruitment effort was eventually abandoned, as these five interviews yielded few useful data and had required 14 school visits (two visits each to seven schools) to achieve. The addition of a shopping voucher as an incentive in year 2 increased the participation rate only very marginally.

The overall finding from the recruitment efforts and results from speaking to these 'non-participating' parents was that there was a lack of understanding of and engagement with the paperwork in various respects. In the initial piloting of the materials, the paperwork such as the information sheet and consent form was found to be very long, even though it had been shortened as much as possible and a graphic design company had produced a very friendly format. Despite this, none of this group of parents could articulate what the study was about in full or mentioned the comparative aspect of SoV, indicating that the paperwork had not communicated the study to parents clearly or that the information had not been retained. One had understood that it was to 'seal their teeth' but thought that it was to address existing holes in children's teeth and one thought that the SoV programme also handed out toothbrushes.

Another thought that it addressed tooth grinding and that it was a student research project. No negative attitudes towards the SoV intervention or trial were expressed.

In interviews, both school and CDS staff discussed similar problems with contacting and recruiting parents for programmes, and commented that they did not always get paperwork back from parents whatever the programme. School and CDS staff thought that parents with little English would also have problems, especially with long forms; of the five non-participating parents recruited for interview through school visits, one had no English (a friend attended the interview to translate) and another spoke English as a second language. CDS staff also mentioned that some parents had problems completing paperwork because of literacy problems. One parent commented they would have preferred to receive information about SoV face to face rather than in a 'big booklet'. School staff thought that some parents needed face-to-face support in order to understand the study and to complete recruitment forms correctly, and so would sometimes assist parents with filling in paperwork. One school staff member commented that it would have been helpful for teachers to know more about SoV so that they could have answered parents' queries about it. Some of the difficulty was also a result of the volume of paperwork and participation in other dental programmes running in the school, leading parents to think that they were already taking part. CDS staff reported that schools often found it a challenge themselves to keep track of the paperwork from different programmes operating in the school, including several dental programmes. School and CDS staff also commented that parents who were already engaged with health and dental services were another group that was less likely to participate because they might not see a need beyond their existing dental visits. One parent commented to the researcher in the playground that their child already saw a dentist and they did not want to use up additional resources unnecessarily. Other families who tended not to engage, according to school staff, were those who were nervous of school environments or who had chaotic lives or work/other commitments that were difficult to juggle. Some school staff thought that parents needed reminders in person from school staff to sign up for programmes. School staff sometimes made an effort to recruit those families, in person, that they thought might be particularly in need of services, either to explain letters or to discuss any potential barriers.

Summary

The work reported in this chapter set out to answer a series of questions (see *Table 68*) that related to the acceptability of technologies under test and the setting in which they were being provided.

The first question related to the acceptability of the FV and FS treatments to the children, what factors influenced acceptability and if there were any possible differences between the trial arms.

Overall, the acceptability of the treatments was very high, as judged by the fact that very few children refused treatments or discontinued in the trial because of the lack of acceptability of the treatments (see *Chapter 3*). When judging acceptability from the perspective of both the parents and the children, it was apparent that this was influenced to a large degree by the wider factors rather than the actual treatments being provided. This means that acceptability needs to be understood as a broad measure, as contextual factors can make a significant difference to acceptability for children, parents and schools.

From the perspective of the children, the novelty of dental treatment in the MDC and MDC aspects such as the provision of reward stickers both seemed to feature as highly in the issues raised in the qualitative interviews as issues around the treatments provided. When pressed specifically on the treatments, the taste of the interventions featured highly in the narratives.

There were significant differences in the acceptability of the FS and FV treatments with the preference changing over the trial period. However, the more involved nature of the FS treatment in the early visits, compared with the constant application of the FV at every treatment visit, is reflected in the results.

The second question concerned implementation, whether or not the delivery of this type of preventative treatment was acceptable to children, their parents, clinicians and the schools in which the treatments took place and the factors affecting implementation of treatment in a school setting.

The answer to this question has to be yes, and it is clear that in deprived areas in which encouraging at-risk children to attend services is key, this work has shown that the school context can be an effective delivery organisation for preventative services. In the qualitative interviews, parents reported trust in the school and convenience of access as important factors in utilising the service.

The child-friendly nature of the setting, the longer-term and ongoing relationship of the CDS with the participating schools and the convenience of attending in school were all factors affecting the acceptability of the treatment setting for parents, teachers and CDS staff.

The favourable reports from the school staff on the implementation of the study and the minimal disruption to the running of the school caused by the CDS team visiting are positive features of the feedback received.

The third question concerned the factors that affect whether or not parents consent to take part in an intervention and trial such as SoV.

A clear and definitive answer to this question was not forthcoming, primarily because of the difficulty in recruiting non-consenting parents. Those who did not want/were insufficiently organised to consent to the trial were similarly difficult to consent to an interview about non-consenting. Trust in the CDS and particularly in the school's judgement about facilitating the trial were raised as important determinants of a positive decision by parents to allow their children to participate in the trial. Tailored communication and assistance with understanding materials and completing forms could help those with low literacy or levels of English to access trial and intervention information to a greater degree.

The fourth question concerned whether or not treatment with FV or FS affects (self-reported) subsequent oral health behaviour, and if so whether or not there differences between trial arms.

In the main clinical analysis of the study (see *Table 13*) and qualitative analysis, there were no significant differences between trial intervention arms related to tooth brushing, diet or other oral health-related habits. In the qualitative interviews, some parents reported that the fact that their child was participating in the trial heightened their awareness of dental issues, but it is clear from the quantitative analysis that these parameters did not impact significantly on trial outcomes.

What is the effect of the trial on recruitment or acceptability to parents, dental staff and schools?

The reasons offered by parents for consenting their children to the trial included the perceived benefits. However, it is clear that, on occasion, parents were not entirely clear about or could not fully recall the purpose of the trial, again resorting to trust in the school and familiarity with the CDS.

The main trial findings and conclusions are discussed in *Chapter 6*.

Chapter 6 Discussion and conclusions

Main trial findings

Clinical results

This trial found that the proportion of children who developed dentine caries or had a restoration or tooth extracted because of caries (D_{4-6} MFT) on any FPM after 36 months did not differ significantly between those treated with FS and those treated with FV (OR 0.84, 95% CI 0.59 to 1.21; $p = 0.351$). Similarly, when the proportion of teeth, the number of teeth or the number of tooth surfaces was studied as the outcome measure, no significant difference was observed between treatments. However, across all of these measures, marginally fewer teeth were affected in the FV-treated children.

This study was commissioned because the relative effectiveness of FS and FV was unknown. Cochrane systematic reviews published just before¹⁷ this study started and immediately before it finished¹⁶ came to the conclusion that, when comparing resin-based FS and FV application, there is some evidence to suggest that FS is more effective. However, these studies reported that it is not possible to draw definitive conclusions based on the four previous studies to have compared resin-based FS and FV. The authors attributed this to scarce and clinically diverse data, and to the low quality of previously reported studies.

What other studies found

There have been four previous studies that have investigated whether resin-based FS or FV is the more clinically effective.^{61,66-68} In their 2016 review of these studies, Ahovuo-Saloranta *et al.*¹⁶ said that it was not possible to reach conclusions about whether to apply FS or FV to the occlusal surfaces of permanent molars to best effect. The clinical outcomes from the current trial suggest that there is no significant difference in the clinical outcome, irrespective of whether FS or FV is used.

In this study, care was taken to ensure that potential confounding factors were accounted for in the analyses. These were adjusted to account for the deprivation score of the locality in which the schools were located, the size of the school and individually reported oral hygiene regime, diet and dental attendance. None impacted on the clinical finding of no significant difference between the FS and FV treatments in terms of clinical effectiveness.

It is, therefore, necessary to take into account cost and patient acceptability considerations, as discussed in *Health economics* and *Treatment acceptability*.

Other clinical findings

Beyond the primary and main clinical outcomes, some additional clinical parameters were explored.

Surfaces protected

Clearly, the only surfaces that could be protected by the FS were the occlusal surfaces, although the FV had the potential to protect both the occlusal and the non-occlusal surfaces. When diagnosed at the caries into dentine (D_{4-6} MFT) level, there was, as would be expected, a significant difference in the proportion of occlusal surfaces that experienced decay compared with non-occlusal surfaces. However, no significant differences were observed between treatments in relation to the protection afforded to occlusal and non-occlusal surfaces.

The effect of including enamel caries

All of the primary outcome data were based on the traditional caries detection threshold: caries into dentine. In this study, the use of the ICDAS caries scoring system made data available at a lower diagnostic threshold, thereby enabling an analysis that included both enamel and dentine caries. This was the only analysis that

suggested a significant difference in outcome between the FS and FV arms of the trial in favour of the FV-treated children. The inclusion of the D₁₋₃ lesions resulted in a significantly lower proportion of caries lesions in the FV arm than in the FS arm, a finding that may well reflect the caries-protective effect of FV on smooth surfaces. However, this effect is negated by the overall finding of no difference in the proportion of children or the number of teeth or tooth surfaces that developed D₄₋₆MFT lesions, the primary outcome measure.

‘Wash-over’ effect

It is also possible that a ‘wash-over’ effect was observed in the FV arm. In other words, the raised intra-oral fluoride environment associated with the FV treatment may have exerted an effect on teeth distant from the FPMs. However, this proved not to be the case, and no significant differences were observed between treatments when whole-mouth D₄₋₆MFT scores were analysed.

Trial duration

This trial took the traditional approach to the duration of caries clinical trials of 36 months’ follow-up in the absence of radiographic examination. The question arose of whether or not a difference in primary outcome would have been observed with a trial of shorter duration. It was not possible at either the 12-month or the 24-month clinical assessments to demonstrate any clinically significant difference between the FS and FV treatments.

Failure to prevent dental caries

It should be noted that, irrespective of treatment received, around one in five children developed dental caries that had progressed into dentine on at least one FPM. This probably reflects the high caries risk status of the children participating in the trial.

Health economics

The health economics analysis indicated that, within the context of a MDC setting and under the trial conditions, FV cost less than FS, even taking into account the repeated application of FV over the trial period. A similar picture is shown when the costs to the patient and family are included. Although there is no obvious single cost driver that accounts for this cost differential, it appears that the FV arm had a consistent and cumulative pattern of fewer costs in intervention and health-care utilisation and, subsequently, in costs attributed to the family.

When the costs are translated into estimating the impact of delivering FS or FV on NHS budgets, this estimates that FV results in a cost saving of £68.13 per child treated compared with FS.

The clinical findings showed no statistically significant or clinically meaningful differences across the majority of primary and secondary outcomes (including health utilities). In such a scenario, the health economic analysis inevitably becomes a cost-minimisation analysis. Thus, the cost differences and subsequent budget impact could be seen as one of the key findings of the economic analysis. In our sensitivity analysis of the budget impact, changing individual parameters estimated that there could be different results. This further examination of a range of scenarios was undertaken because of the need to fully consider the potential impact of delivering the intervention in a different ‘real-world’ clinical context rather than just under the trial conditions.

With such small and non-statistically significant differences in outcomes, any ICERs become extremely sensitive to small changes in numerical values and should be treated with appropriate caution.

The base-case results show that because numerical differences were very small and not statistically significant, the cost-effectiveness results estimate that, in terms of the cost per child with dentine caries avoided, and for cost per QALY, FV dominates FS. This result (and interpretation) should be treated with

caution, particularly in the CUA, given the very small QALY differences that would be highly unlikely to translate into meaningful benefits to children. In terms of the cost per QALY analysis, there was a very small difference in effect in favour of FS, but, when the ICER was estimated, FV dominates FS. As outlined, the cost-per-QALY analysis should be treated as exploratory.

The CEAC for the CUA shows that, if the NICE guidelines are followed, there would be a 70% probability of FV being at a NICE societal WTP threshold of £20,000 per additional QALY and, as such, FV could be considered cost-effective.

An exploratory model-based analysis undertaken to look at the potential longer-term cost-effectiveness of FS and FV was consistent with the within-trial analysis.

Overall, even taking into account the need for further examination of the impact of missing data, the analysis shows that FV costs less than FS and could result in moderate cost savings to the NHS if it was delivered as the preferred treatment in the prevention of caries in the FPMs of children at high risk of dental caries.

Although the health economic evaluation has focused on reporting the relative cost-effectiveness and budget impact of FS versus FV, understanding the practical implications is important. As shown in *Table 66*, there are hypothetical savings to be achieved, and an estimated additional 93 children could be treated if FV was used rather than FS.

However, such a scenario is too simplistic. Further consideration would be needed to ascertain how this would impact on the service. The MDC is despatched to specific schools with different population sizes, so, although in theory greater child throughput could be achieved, this would be dependent on the number of children available to treat during one session and other logistical issues involved in organising and delivering the MDC service. Other MDC factors would need to be taken into account (e.g. delivering FV may not necessarily require the current vehicle and staff mix). Although the trial showed that FV is less costly than FS, the trial may not reflect real practice in terms of the ability to deliver FS as a one-off treatment compared with repeated applications of FV. Although the scenario analysis reported in *Table 17* of our findings suggests that in such a context FS would be seen as less costly, the clinical effectiveness results achieved were under the trial conditions and, thus, appropriate caution must be placed on any interpretation that the same clinical benefits could be achieved in a different treatment protocol. The importance of child and school factors (such as turnaround of children from the classroom, having to fit with a school timetable and children not wanting the FV applied) would also need to be fully considered.

An important question to address next would be 'what does this mean in practice in terms of service design, capacity and planning?'. There is an opportunity to take this research further by applying the trial results to an expansion of the health economic analysis to allow the modelling of plausible scenarios to support decision-makers and the dental clinical community, translating the findings from this trial into optimal models of service delivery for preventative dental health in children.

Strengths and limitations of the health economic analysis

This health economic analysis has been undertaken as part of a rigorous randomised trial to assess the clinical effectiveness and cost-effectiveness of FS and FV delivered within a MDC. Data were collected prospectively alongside the trial with the economic evaluation, which was an integral component of the trial design from the outset. It also benefits from reporting a budget impact analysis. Any changes to funding arrangements in health care over the next 5 years and the impact of any decision on local and national NHS dental budgets can now be informed by our findings. However, some limitations are acknowledged, particularly in relation to undertaking health economic evaluations in this context, and should be fully considered.

Consideration of the longer-term impact of fissure sealant versus fluoride varnish in preventative dental health programmes

Exploration of the longer-term costs and outcomes of the two technologies was an important consideration in developing the health economic analysis, given that this was done as a preventative intervention to improve the longer-term dental health of children who are at high risk of caries. A Markov model was built and validated with the trial clinicians as commensurate with the expected caries pathway as a result of having preventative treatment with FS or FV. The results show that FV remains dominant over FS, with this result remaining reasonably robust in the sensitivity analysis. However, caution must be exercised when interpreting these results.

The model-based analysis beyond the trial period was significantly hampered by the lack of evidence of the longer-term costs and outcomes in order to populate the model. The Cochrane review¹⁶ highlighted the lack of data available to compare FS and FV applications; only one study provided any data beyond our trial period,⁶¹ but this was limited by several biases, particularly the fact that only a limited number of children were followed up in the longer term. Only informed assumptions could be made about the longer-term costs and outcomes of FS versus FV based on clinical opinions from the trial team, informed by the trial results. Although it could be argued that, in the absence of good-quality evidence, the feasibility of modelling outside the trial period is questionable, this has been done to ascertain the framework for a model-based economic analysis and, importantly, the evidence that would be needed to populate the model. In the absence of data from previous trials, undertaking further follow-up of the trial cohort could provide an excellent opportunity to formally address the question of the longer-term clinical effectiveness and cost-effectiveness of FS versus FV.

Choosing and using appropriate health outcomes to inform the health economic analysis

An important issue that has arisen from this study is the need to give thorough attention to the outcomes of interest for the health economic analysis. A plethora of literature has examined oral health outcomes in the adult population but, in comparison, the evidence base for children is sparse. The strength of our evaluation is that we choose three outcomes that we expected to provide a comprehensive picture of costs and outcomes of the two technologies to support decision-making, both from a UK NHS decision-making perspective and in the clinical dental community.

Providing an estimation of the incremental cost per QALY is seen as the cornerstone of demonstrating cost-effectiveness within a UK NHS context. For example, the NICE reference case for health technology assessment⁵⁷ highlights the inclusion of a QALY as its health outcome of choice. When the trial was originally conceptualised, a pragmatic decision had to be made on which measure to use, given the paucity of measures available for children and, in particular, the lack of evidence in the utility of generic HRQoL measures. We decided, after discussion with the developer and following recommendations made by the Health Technology Assessment funding panel, to use the CHU-9D, even though it had only just been published and its utility in a dental health context was still unknown. CHU-9D score was not measured at baseline; however, as this was a randomised trial, it is reasonable to assume that any differences between the two groups at that point were due to chance. The inability to consider utility curves over outcome time points only, rather than including baseline, could be seen to result in a reduction in power, but, given the preventative nature of this study (i.e. the study was not missing assessing utility during an episode of illness) and the fact that there were assessments of utility on multiple occasions, this is unlikely to be a major issue.

A study published since the start of the trial suggests that CHU-9D can be used in children aged 6 or 7 years.⁵³ That work, which considered the psychometric performance of the CHU-9D versus the EuroQoL-5 Dimensions Youth version, suggested that children at this age can understand and complete the measure. This supported our own informal and limited evaluation of the CHU-9D that was undertaken prior to the start of the trial. The CHU-9D was assessed in the context of a child dental community clinic in New Zealand⁵⁴ and was found to have the potential to capture HRQoL across different caries experience, showing that those with no apparent caries had a higher mean score than those with caries (0.88 vs. 0.87, SD 0.10), although the difference was small. Interestingly, this cross-sectional sample had lower HRQoL

scores than our trial sample, although it is difficult to assess whether or not the patient populations are comparable. In terms of QALYs generated, this study reported that the difference in QALYs between those with and those without caries was 0.12. This is a fairly moderate difference, but it could suggest the potential of the CHU-9D to identify small but important changes in QALYs as a result of caries. Because of the lack of clinical differences in caries between our trial arms, we were unable to detect differences in utilities and QALYs. Subsequently, Foster Page *et al.*⁶⁹ undertook a randomised controlled trial to further assess the CHU-9D in terms of its responsiveness to changing components of the decayed, missing, filled tooth surfaces in primary dentition (dmfs) and DMFS scores in children aged 6–10 years over a 1-year period. They found that the mean CHU-9D improved from 0.88 to 0.9 from baseline to follow-up, with no significant difference found between caries status and CHU-9D. Again, CHU-9D scores from their study are lower than those in the present trial and lower than those in other studies, such as the 0.86 reported in the Canaway and Frew study,⁵³ indicating that, as in this study, the impact of children receiving dental care under trial conditions cannot be ruled out. Similar to the later Foster Page *et al.* study,⁶⁹ this trial suggests that the CHU-9D is insufficiently responsive to changes in caries experience.

An important question is ‘what could be done to improve measures aimed at capturing HRQoL in relation to this patient population?’. Whether the focus should be on generic HRQoL measures or on condition-specific measures is the subject of much debate, and it is important also to consider the context of this trial within a preventative/public health context. For example, the NICE public health guidance⁷⁰ recognises the possible challenges of undertaking a CUA, and other approaches such as a cost–consequence analysis could be considered, although CUA is advocated (along with the need for HRQoL measures that can derive appropriate utilities) to ensure comparability across other parts of NICE.

The authors suggest that patient-reported outcome measures (including HRQoL) for use in a dental public health context should have a stronger conceptual and methodological basis. Understanding children’s preferences for treatment, the properties of measures and the association that these have with (1) dental-related health and (2) HRQoL warrants careful attention. Moreover, understanding and capturing the utility/disutility associated with caries experience over time will assist in ensuring longer-term examination of the cost-effectiveness of different strategies.

The cost-per-QATY analysis undertaken in this trial allows the consideration of a dental health state utility, which has been suggested as a more meaningful measure in the context of dental health. Although the QATY has been reported in studies,^{31,71} there has been little ‘methodological movement’ since the original work.^{55,72} In this trial, published utilities were used alongside clinical opinion from the trial team to attribute a utility to (1) each individual tooth and (2) a composite QATY drawing on other studies³¹ and preliminary work undertaken as part of a NICE public health guideline.⁵⁶ The present analysis suggested that QATY gain was greater with FS than with FV, suggesting that FS could potentially be cost-effective. The results should be viewed with appropriate caution, given the approach taken to derive the number of QATYs. QATY gain appears to be a potentially useful dental health outcome, and further work is recommended to improve the underpinning work to derive suitable utilities for calculation of QATYs.

The importance of collaboration between health economists and the dental health research and clinical community will be instrumental to improving the quality of economic evaluations within preventative dental health.

Treatment acceptability

That so few participants withdrew from the study (as opposed to simply moving to a non-participating school) is in itself evidence that both treatments are acceptable. That is not a novel finding. These treatments have been in routine clinical use since the 1960s and have been received by a great many children around the world.

However, there are some interesting observations from the process evaluation reported in *Chapter 5* that are likely to be of value in considering the future provision of these technologies in community programmes. Evaluation using the DTF scale correlated with the intensity of the treatment, with those receiving FV being significantly happier at baseline and this situation being reversed at the 30-month treatment session. This presumably reflects the fact that at baseline the FS-treated children had to spend longer in the dental chair than those receiving the FV treatment. The FS recipients were also subject to the use of three-in-one syringes and aspirators; in contrast, in the FV arm, treatment consisted of the simple act of placing cotton wool rolls in the mouth and painting the FV onto included FPMs. At the final treatment session, children in the FS needed treatment only if a FS had been lost, was judged to be incomplete or required top-up. In contrast, in the FV arm the time required in the chair was similar to that required for the baseline examination.

The feature of both treatments that was most remarked upon during the interviews was taste. This is interesting because in clinical teaching dental professionals, perhaps using 'tell-show-do' techniques, are taught to explain the sensations and experiences to a child before treatment. Clearly, an explanation of what may be expected in terms of taste when treating children is an important element of preparing them for treatment.

However, it is clear from the qualitative work carried out in this study that it is not so much the treatments themselves that children remember but rather the wider issues surrounding the treatments. Reward stickers, the movement of the dental chair (the chair was routinely reclined to allow children to have both the dental clinical examination and the treatment) and the coloured protective glasses that the children were required to wear all featured highly in their narratives of the experience. The novelty of the MDC visiting the school and the opportunity to have a break from the routine of daily life in the classroom also featured as a factor affecting acceptability. It was, however, interesting that in the later stages of the trial, when the children were aged 9 or 10 years, time away from the classroom and having to catch up on work did become a minor issue for some. In the course of the trial, the children would have visited the MDC on up to 10 separate occasions (four dental examinations and six treatment visits), so by the end it would have been a fairly routine experience. These findings about the broad range of factors that contributed to the acceptability of treatment for children indicate that delivery via a child-friendly service in a school setting is an important consideration for implementing this type of preventative dental treatment.

As this trial was based on the existing Designed to Smile programme, it is likely that the initial visit may not have been the child's first experience of the MDC. Consent to participate in the trial was, however, considerably lower than the normal uptake of treatment offered by the CDS. The reason for this is unclear. Participating and non-participating parents who were interviewed were almost universally positive about the intervention, and reasons for non-participation are therefore likely to be a result of factors other than acceptability. A small number of parents appear to have not participated because their children were already receiving similar treatment and they wanted to continue with this. A more common reason for non-participation appears to be the difficulty of communicating effectively with parents via written information delivered through schools in areas of socioeconomic deprivation. Obviously it is necessary to ensure that parents and carers are adequately informed before making a decision about their child's participation in a clinical trial and in particular in a CTIMP. The trial team worked hard with our PPI partners to ensure that the information was provided in as non-threatening and user-friendly a way as possible, for example by incorporating the logos and colours of the usual Designed to Smile programme patient-facing materials.

In the interviews exploring participation in the trial and in the piloting of materials, some interviewees discussed difficulties in English or literacy that may have affected the ability of parents to read and complete paperwork for the trial. This is likely to be a factor in participation rates in other areas of socioeconomic disadvantage or areas where there is a high proportion of residents whose first language is not English. A considerable amount of information was required to be offered to the parents and carers of potential participants. This would have been in addition to other paperwork that schools send home to parents; some interviewees mentioned that the volume of paperwork could also be a barrier for some parents, either because they did not keep track of it all or because there was too much to read.

The information on details of the trial that had to be included in the paperwork for SoV may have contributed to this.

Trial fidelity

In any clinical trial, adherence to the clinical protocol (fidelity) is an important consideration. Aspects of this are now discussed.

Number of treatments received

In the course of the trial, participants were scheduled to receive treatment on six occasions. Clearly, the number of treatments received, whether application of FV at each visit or check-up or, if necessary, 'top-up' of the FS, is important. More than 70% of children attended all six treatment visits, and 95% of children in the FS and FV arms of the trial attended at least five treatment visits, which is excellent adherence to the scheduled treatment protocol. The CACE analysis demonstrated that such a high level of compliance means that adherence to the treatment protocol was not an influencing factor in the results obtained at 36 months. To obtain such a level of compliance reflects the relationship between the CDS team, the schools and their parents.

The CACE analysis was performed as a sensitivity analysis in order to explore the effect of attendance for treatment on treatment efficacy. A CACE analysis is preferable to a per protocol analysis, as it respects the trial randomisation, but is usually more suited to trials with two active arms rather than trials with one active trial arm and one control arm. Hence in SoV, the FS arm was selected as the 'control' treatment for the CACE analysis, as ideally it is a one-off treatment whereas FV needs to be applied regularly for full effectiveness. It was also the current standard treatment for children in these schools. The results indicated that, in fact, there was very little variation in treatment adherence, with the majority of children attending either five or all six FV treatments. As such, the CACE analysis indicated only slight gains in treatment efficacy with additional visits. In a wider context, this means that, for FV to be effective in the community as a caries prevention tool, treatment adherence needs to be ensured.

Treatment window

The six treatment appointments were scheduled at 6-month intervals over the course of the trial. Owing to the practicalities of scheduling visits of the MDC to schools to accommodate holidays and acknowledging that there were days when it was not convenient for the schools to host the MDC and so forth, it was agreed at the outset that a treatment window of 4 weeks either side of the treatment due date would not compromise the integrity of treatment delivery and would reflect the practical nature of a pragmatic clinical trial such as SoV. Over the course of the trial, adherence to this schedule was good. Overall, in 71.6% of schools, all treatment visits were within the treatment window, and in a further 26.1% of schools, only one of the six treatment visits was outside the schedule. This further indicates the fidelity of the trial.

Fissure sealant retention

The level of FS retention in this study was very high. This is because the study participants were seen at 6-monthly intervals and FS was 'topped up' if deficient. Furthermore, in the case of the maxillary FPMs, the teeth were sealed if part of the mesial-occlusal pit and fissure was erupted and the distal aspect was then sealed at a subsequent 6-month visit. At the 30-month treatment visit, only a small proportion of previously sealed teeth were reported as being 'lost', with 74% of upper teeth and 88–91% of lower teeth reported as 'partial', that is, sealant did not cover the whole of the occlusal surface.

Crossover

One deviation from protocol was observed. At the 12-month treatment visit, one child who had been randomised to the FV arm received FS. This was logged and the child continued in the trial in the arm to which they were randomised.

Examiner reproducibility

Throughout the trial, efforts were made to ensure that the dentists undertaking the clinical examinations were appropriately trained and calibrated. A professor of paediatric dentistry who was involved in the development of the ICDAS index trained the examiners at baseline and a second professor of paediatric dentistry undertook the annual training and calibration exercise before each round of examination began. The kappa scores achieved indicated that all examiners demonstrated a high level of intra-examiner reproducibility, and that inter-examiner reproducibility was also high.

Study considerations

From the issues previously discussed, the authors are of the view that this was a very robust and well-conducted study. The trial protocol was rigidly adhered to and compliance was excellent, as were follow-up and completion rates. Fidelity was as high as could possibly be expected. The trial team are content that there was nothing that they would have done differently in answering the question proposed at outset. Some aspects of the trial are considered further here.

Study numbers

The caries risk status of the participants is an important consideration. The SoV trial was set in areas of social and economic deprivation and more than half of the participants had decay into dentine in their primary dentition at the start of the study. The finding that approaching one in five of the participants experienced dental caries in at least one FPM at 36 months, across trial arms, makes clear that the study population was appropriate and typical of those whom the technologies tested are designed to benefit. The consistent finding from the regression analysis of caries experience in the primary dentition at baseline being a significant predictor of caries in the permanent dentition is as would be expected.⁷³ This of course did not affect the conclusions about differences in the relative caries-protective effect of FS and FV.

It is clear that the randomisation and stratification procedure employed was very successful and that the trial arms were well balanced at baseline.

The trial was more than adequately powered. This arose for the following reason. Calculations based on a previous study in South Wales and estimates of treatment effectiveness suggested that 313 participants were required per arm. The original intention was to recruit all participants in the same school year. However, this effectively meant recruiting all children in the period September–December in the first school term in order that the 6-monthly treatment visits could be accommodated. By December just over 500 children had been recruited, too few to satisfy the power calculations. With the funder's support, recruitment was extended to a second school year. This resulted in two study cohorts, each of which was followed for 36 months. There was no observed cohort effect on the clinical outcome.

In planning the study, allowance was made for an 8% withdrawal per annum. In the event, many fewer children were lost from the study, with the most common reason for failure to complete the study being moving away from the area or to a different school that was not participating in the trial. When children moved to a participating school they continued in the trial. Recruitment to the trial in the second cohort proceeded at a much quicker pace than in the first year and so the study over-recruited by around 100 participants. The view was taken that, having invited the parents of the children to participate in the study, it would have been problematic to refuse the opportunity to participate to already consented children.

This, together with the much lower than expected dropout rate, meant that in both trial arms the number of children completing was in excess of the numbers required to satisfy the power calculation.

Questionnaire return rate

Information to inform oral health-related habits and the health economics utility scores was collected via a self-complete questionnaire. The efforts taken to maximise the return rate are described in *Chapter 2*. The revised follow-up strategy was found to boost return of the follow-up questionnaires, with the overall return rate of the DHQ rising to 60% for the whole trial.

Clearly, this limited the number of participants who were available for the secondary analyses, which were dependent on information on covariates gained via the questionnaire. However, there was no evidence of a difference in return rates between treatment arms. It should be remembered that this trial was conducted in Community First areas, which are areas designated by the Welsh Government as being of high social and economic deprivation. A response rate of 60% is probably as good as can be expected in this setting.

Adverse events

Care was taken in recruitment to the trial to exclude any participants with a known history of allergy to colophony, a constituent of the FV, and also those with severe asthma, that is, those who had ever been admitted to hospital overnight for the treatment of asthma. No adverse events were observed or reported in relation to the use of either FS or FV, and it is concluded that these treatments are suitable for use in children aged between 6 and 10 years.

Implications for health care

This is the largest ever study to address the question of the clinical effectiveness and cost-effectiveness of FS and FV. The very high standard to which this work was conducted and the excellent fidelity obtained mean that the findings reported here are robust.

Given that the previous systematic reviews of the clinical effectiveness of the technologies tested suggest that FS may be clinically superior, the results obtained in this trial are perhaps contrary to what many paediatric and public health dentists would have expected.

The SoV trial has clearly shown that, although at 36 months fewer than one in five children had developed decay into dentine in their FPMs, there was no clinically important difference in the proportion of children developing decay (D₄₋₆MFT) on any FPM whether treated with FS or FV. That leads to the question of costs.

The health economic analysis suggests that the costs favour FV. The budget impact analysis at 3 years showed that FV resulted in a cost saving of £68.13 per participant over the 3-year period compared with FS.

Both treatments are acceptable and the qualitative work undertaken has shown that factors other than the treatments themselves are uppermost in the children's recollection of having received the treatments. The very low numbers of children stopping treatment is further proof of the acceptability of FS and FV when placed in the context of a community dental programme using MDCs. This type of intervention delivered in a school setting was also found to have high acceptability for parents and school staff.

Implications for research

There are number of research questions and issues that arise from this work.

The findings from this robust study will add to the evidence base of the Cochrane review of relative effectiveness of FS and FV. The Cochrane review should consequently be updated.¹⁶

In the trial, the FS was applied when the FPMs first erupted and was maintained throughout the trial and the FV was applied at 6-monthly intervals. A key question, given the results obtained, and now that active treatment intervention has been discontinued, is whether or not the caries-protective effects of FS and FV will remain the same over the coming years. Presumably, the FS will remain for some months and years to come, at least in the depths of the pits and fissures. As a result, a difference in the preventative effects

may become apparent after, say, a further 2 or 3 years. It would be useful to re-examine the participants in the school in 2017/18 in order to determine the effectiveness of the treatments after 5 and 6 years.

Logistics and cost limited this trial to a comparison between FS and FV. A third option that was considered by the research team was the inclusion of a third arm applying both FV and FS; this would have proven cost prohibitive. Whether or not such an approach is merited in future research is debatable.

In relation to trial fidelity, to our knowledge, this work is the first to apply CACE analysis in a dental trial. More work to understand this technique in the context of dental clinical trials with two active treatments would be advantageous.

Regarding the health economic element of the work, an important question is what could be done to improve measures aimed at capturing HRQoL in relation to this patient population. Whether the focus should be on generic HRQoL measures or condition-specific measures is a subject of debate, and it is also important to consider the context of this trial within a preventative/public health context. For example, the NICE public health guidance⁷⁰ recognises the possible challenges of undertaking a CUA and that other approaches such as cost–consequence analysis could be considered, although CUA is advocated (along with the need for HRQoL measures that can derive appropriate utilities) to ensure comparability with other parts of NICE.

We suggest that there is a need for a greater conceptual and methodological basis to patient-related outcome measures (including HRQoL) for use within a dental public health context. Understanding children’s preferences for treatment, the properties of measures and the association that these have on (1) dental-related health and (2) HRQoL warrants careful attention. Moreover, understanding and capturing the utility/disutility associated with caries experience over time will assist in ensuring longer-term examination of the cost-effectiveness of different strategies.

The cost per QATY analysis undertaken in this trial allows the consideration of a dental health state utility, which has been suggested as a more meaningful measure in the context of dental health. There has been little ‘methodological movement’ since the original work.⁵⁵ In this trial, we used published utilities and sought clinical consensus to (1) attribute a utility to each individual tooth and (2) create a composite QATY drawing based upon other studies³¹ and preliminary work undertaken as part of a NICE public health guideline.⁷⁰ The present analysis suggested that FS derived more QATY gain than FV, suggesting that this could result in FS being potentially cost-effective. However, it is important that appropriate caution is exercised when considering these results, given the approach taken to derive the QATY. However, the QATY appears to be a potential useful dental health outcome and further work is recommended to improve the underpinning work to derive suitable utilities for the calculation of the QATY.

The importance of collaboration between health economists and the dental health research and clinical community will be instrumental to improve the quality and subsequently drive up the quality of economic evaluations within preventative dental health.

Conclusions

The findings of this trial demonstrate that in community oral health programmes targeted at children at high caries risk, the application of FV as a caries preventative measure will result in caries prevention that is not significantly different from that obtained by applying and maintaining FS after 36 months. There is a cost saving of £68.13 per child treated, using FV compared with the application of FS over this time period. Both treatments are acceptable to children aged 6–10 years; perceptions of undergoing treatment are influenced by aspects of treatment (especially taste) but also by wider factors associated with a child-friendly MDC. Acceptability to parents and to schools was also high.

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Contributions of authors

The following named authors contributed to the development of the research question and study design, study implementation (including members of the trial management group), analysis and/or interpretation of data and submission of the final report. Details of specific individual roles are below.

Ivor Gordon Chestnutt (Professor and Honorary Consultant in Dental Public Health; Co-Chief Investigator, lead applicant and the guarantor for the study) led the development of the research proposal, was the principal link between the research and clinical teams and led the final report preparation and submission.

Simon Hutchings (Trial Manager, December 2010 to December 2014) prepared the trial protocol, led permissions approvals and was a link between the Clinical Trial Unit and CDS.

Rebecca Playle (Senior Lecturer in Medical Statistics; Coapplicant and Senior Trial Statistician) led the development of the statistical plan and the analysis of the trial.

Sarah Morgan-Trimmer (Research Associate) was responsible for the qualitative element of the process evaluation.

Deborah Fitzsimmons (Professor of Health Economics; Coapplicant and Lead Health Economist) was responsible for the health economic analysis.

Nadine Aawar (Senior Trial Manager, April 2015 to March 2016) was responsible for trial governance-related issues.

Lianna Angel (Data Manager) was responsible for data management.

Sharron Derrick (CDS Manager, April 2014 to March 2016) liaised with schools and co-ordinated the clinical teams.

Cheney Drew (Trial Manager, April 2015 to March 2016) carried out trial management and was a link between stakeholders and regulatory bodies.

Ceri Hoddell (Senior Dental Officer; Coapplicant and Principal Investigator, Cardiff and Vale UHB and Clinical Advisor) was responsible for the oversight of clinical sites.

Kerenza Hood (Professor of Medical Statistics; Coapplicant and Head of the Clinical Trials Unit) contributed to trial design and was a statistical advisor.

Ioan Humphreys (Research Officer) was responsible for the Health Economics Analysis.

Nigel Kirby (Administrative Assistant, April 2011 to June 2012) was responsible for administration during trial set-up, baseline and 6-month treatments.

Tin Man Mandy Lau (Junior Statistician) assisted with the statistical analysis.

Catherine Lisles (Data Manager) was responsible for data management and interim trial management duties.

Maria Zeta Morgan (Senior Lecturer in Dental Public Health) was responsible for the quantitative aspects of patient acceptability.

Simon Murphy (Professor in Public Health Improvement) was responsible for the oversight of quantitative elements of the work.

Jacqueline Nuttall (Senior Trial Manager, April 2011 to June 2013) was responsible for trial governance-related issues.

Kateryna Onishchenko (Research Assistant) was responsible for the Health Economics and developed the health economic model.

Ceri Phillips (Professor of Health Economics) was a health economics advisor.

Timothy Pickles (Statistician) was responsible for statistical analysis.

Charlotte Scoble (Administrative Assistant, July 2012 to March 2016) acted as administrative assistant in support of the trial.

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Barbara Lesley Chadwick (Professor and Honorary Consultant in Dental Public Health; Co-Chief Investigator and guarantor for the study) led the clinical components of the research proposal and was responsible for the training and calibration of the study clinicians.

Study protocol

The protocol for this study has been published²⁰ and is available at www.biomedcentral.com/1472-6831/12/51.

Trial Steering Committee membership

Professor Lorna MacPherson (Chairperson), Professor of Dental Public Health at the University of Glasgow.

David Thomas, Chief Dental Officer at the Welsh Government.

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Mrs Yasmine Pike, Service User Representative.

Independent Data Monitoring Committee membership

Professor Helen Worthington (Chairperson), Professor of Evidence Based Care at the University of Manchester.

Professor Chris Deery, Professor of Paediatric Dentistry at the University of Sheffield.

Mrs Nicola Williams, Primary School Head Teacher at Deri Primary School.

Data sharing statement

We shall make data available to the scientific community with as few restrictions as feasible, while retaining exclusive use until the publication of major outputs. Data will be available via the corresponding author.

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Appendix 1 Research Ethics Committee approval



GIG
CYMRU
NHS
WALES
Canolfan Gwasanaethae
Busnes
Business Services
Centre

Research Ethics Committee for Wales

*Ymchwil Ethegau Aml-Ganolfan yng
Nghymru*

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17 Ffordd Churchill
Caerdydd, CF10 2TW**

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**Website / Gwefan :
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**Sixth Floor, Churchill House
17 Churchill Way
Cardiff, CF10 2TW**

**Telephone : 029 2037 6829
Fax : 029 2037 6824**

15 February 2011

Professor Ivor Chestnutt
Cardiff University
Cardiff University Dental School
Heath Park,
Cardiff CF14 4XY

Dear Professor Chestnutt

Study Title: Seal or Varnish? A Randomised Trial To Determine The Relative Cost And Effectiveness Of Pit And Fissure Sealants And Fluoride Varnish In Preventing Dental Decay
REC reference number: 11/MRE09/6
Protocol number: SPON766-09
EudraCT number: 2010-023476-23

The Research Ethics Committee reviewed the above application at the meeting held on 10 February 2011. Thank you for attending to discuss your application with the Committee.

Ethical opinion

Professor Chestnutt attended to discuss his application with the Committee. He was accompanied by Dr. Simon Hutchings, Trial Manager.

Members present commended Professor Chestnutt on the quality of the information sheets, agreeing that in particular those for children were of a very high standard.

Explanation as to why there is no statistician on the Data Monitoring Committee (DMC).
Professor Chestnutt informed the Committee that the Chair of the DMC is a statistician.

Members present noted the comments on the application regarding the use of tick boxes on the consent form rather than initial boxes, and asked for further explanation of this.
Professor Chestnutt explained that they were trying to simulate what happens in current practice where parents are used to ticking boxes.
Members present agreed this did not present an ethical issue and that the boxes could be ticked.

Explanation as to why non-participants would be interviewed.

Professor Chestnutt explained that they were seeking to interview twenty people who had declined to take part as they wanted to understand why : is it due to the paperwork sent out deterring people or is it due to concerns regarding the use of fluoride. He further explained that they would be sensitive towards approaching these people and that it would be done via parent-teacher groups. Professor

Please note the new address for the REC for Wales at the header of this letter

rhan o Addysgu Bwrdd Iechyd Lleol Powys / part of Powys Local Teaching Health Board

Chestnutt informed the Committee that if they decided to go ahead with this aspect of the study they would submit the documentation as a substantial amendment.

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

The Committee has not yet been notified of the outcome of any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. I will write to you again as soon as one Research Ethics Committee has notified the outcome of a SSA. In the meantime no study procedures should be initiated at non-NHS sites.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

For NHS research sites only, management permission for research ("R&D approval") should be obtained from the relevant care organisation(s) in accordance with NHS research governance arrangements. Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at <http://www.rdforum.nhs.uk>.

Where the only involvement of the NHS organisation is as a Participant Identification Centre (PIC), management permission for research is not required but the R&D office should be notified of the study and agree to the organisation's involvement. Guidance on procedures for PICs is available in IRAS. Further advice should be sought from the R&D office where necessary.

Sponsors are not required to notify the Committee of approvals from host organisations.

Clinical trial authorisation must be obtained from the Medicines and Healthcare products Regulatory Agency (MHRA).

The sponsor is asked to provide the Committee with a copy of the notice from the MHRA, either confirming clinical trial authorisation or giving grounds for non-acceptance, as soon as this is available.

Other conditions specified by the REC

- The word "important" should be removed from the sixth line of the letter / consent form for the examination for training purposes.
- Page four of the information sheet states the study has been reviewed by South East Wales REC. This should be corrected to read the REC for Wales.

If you would find it helpful to discuss any of the matters raised above or to seek further clarification from a member of the Committee you are welcome to contact the REC co-ordinator, Dr. Corinne Scott, whose contact details can be found in the header of this letter.

It is responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Protocol	1	11 January 2011
Participant Information Sheet: Children	1	12 January 2011
GP/Consultant Information Sheets	1	12 January 2011
REC application	signed in ink by Professor Chestnutt and in ink by Dr KJ Pittard-Davies, sponsor's representative	13 January 2011
Participant Consent Form	1	12 January 2011
Summary of product characteristics	Duraphat 50mg / dental suspension; date of revision of text - February 2003	
Annual exam follow up letter	1	12 January 2011
Participant Information Sheet: Parents	1	12 January 2011
Investigator CV	Professor Chestnutt	11 January 2011
Baseline exam follow up letter	1	12 January 2011
Evidence of insurance or indemnity	Zurich Municipal certificate of insurance - Cardiff University - expires 31 July 2011	27 July 2010
Covering Letter	signed Simon Hutchings	13 January 2011
Summary/Synopsis	Participant flow chart; version 1	12 January 2011
Letter from Sponsor	signed DR KJ Pittard-Davies, Cardiff University	11 January 2011
Medical history form	1	12 January 2011
Letter from funder - NIHR HTA programme		21 October 2009
Letter from chief investigator to NIHR HTA		06 November 2009
Interim follow up letter	1	12 January 2011
Missed treatment follow up letter	1	12 January 2011
Example participant material from current Designed To Smile programme		

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

Dr. Brown declared an interest but remained present : Professor Chestnutt is a colleague.

Statement of compliance

This Committee is recognised by the United Kingdom Ethics Committee Authority under the Medicines for Human Use (Clinical Trials) Regulations 2004, and is authorised to carry out the ethical review of clinical trials of investigational medicinal products.

The Committee is fully compliant with the Regulations as they relate to ethics committees and the conditions and principles of good clinical practice.

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Service website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Progress and safety reports
- Notifying the end of the study

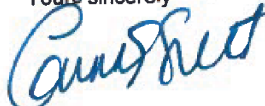
The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email referencegroup@nres.npsa.nhs.uk.

11/MRE09/6	Please quote this number on all correspondence
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With the Committee's best wishes for the success of this project

Yours sincerely



Dr Gordon Taylor
Chairman

Email: corinne.scott@wales.nhs.uk

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments "After ethical review – guidance for researchers"

Copy to: Dr Simon Hutchings

REC for Wales**Attendance at Committee meeting on 10 February 2011****Committee Members:**

Name	Profession	Present	Notes
Dr Gail Boniface	Occupational Therapist	Yes	
Dr Paul Brown	Radiographer	Yes	
Dr Maurice Buchalter	Alternate Vice Chairman / Hospital Consultant (Cardiologist)	Yes	
Dr Kate Bullen	Psychologist	Yes	
Mrs Monika Hare	Research Fellow	Yes	
Ms Nicola Heales	Solicitor	No	
Mr HAO Hughes	Pharmacist	Yes	
Dr Meriel Jenney	Hospital consultant (Paediatric oncologist)	No	
Mr Keith Jones	Retired Probation Officer	Yes	
Dr Mohammad Obaidullah	GP	No	
Ms Susan Pope	Communications / PR	No	
Dr V. Bapuji Rao	Hospital consultant (Psychiatrist)	Yes	
Ms Paula Strong	Nurse	Yes	
Dr Gordon Taylor	Chairman / Statistician	Yes	
Mrs Wendy Turkie	Nurse	Yes	
Dr Richard Walker	Deputy Director	Yes	
Dr Pete Wall	Vice Chairman / Clinical Physiologist	Yes	
Mr Stewart Williams	Management Consultant	Yes	

Also in attendance:

Name	Position (or reason for attending)
Dr Corinne Scott	Co-ordinator
Mrs. Helen Williams	Assistant Co-ordinator

Written comments – not regarding this application - received from:

Name	Position
Dr Meriel Jenney	Hospital consultant (Paediatric oncologist)

**National Patient Safety Agency**

National Research Ethics Service

**CLINICAL TRIALS OF INVESTIGATIONAL MEDICINAL PRODUCTS IN
HUMAN SUBJECTS****After ethical review – guidance for sponsors and investigators**

This document sets out important guidance for sponsors and investigators on the conduct and management of medicinal trials following ethical review. The guidance is supplementary to the ethical opinion provided in the letter from the ethics committee. However, some reporting procedures described below are statutory requirements under the Medicines for Human Use (Clinical Trials) Regulations 2004 ("The Regulations"); this is indicated in the text. Failure to comply with these requirements could lead to the committee changing its opinion and recommending to the Medicines and Healthcare products Regulatory Agency that the clinical trial authorisation should be suspended or terminated.

1. Further communications with the Research Ethics Committee
 - 1.1 Further communications during the trial with the Research Ethics Committee that gave the favourable ethical opinion (hereafter referred to in this document as "the Committee") are generally the responsibility of the lead sponsor. However, the sponsor may delegate responsibility to the Chief Investigator or another representative.
 - 1.2 Where there is more than one sponsor for the trial, it is recommended that the lead sponsor or its representative takes responsibility for all communications with the Committee. However, one of the co-sponsors may take responsibility for each of the following group of functions:
 - Substantial amendments, modified amendments and the conclusion of the trial
 - Urgent safety measures
 - Pharmacovigilance reporting.

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2. Commencement of the trial

- 2.1 It is assumed that the trial will commence (i.e. the initiation of any protocol procedures) within 12 months of the date of the favourable ethical opinion.
- 2.2 Under the Regulations the sponsor must obtain Clinical Trial Authorisation (CTA) from the Medicines and Healthcare products Regulatory Agency (MHRA) before the commencement of the trial. Evidence of the CTA should be forwarded when available (if not already provided to the Committee). Where the MHRA requests significant changes to the protocol before confirming CTA, or attaches any other condition requiring substantial amendments to be made to the terms of the REC application or the supporting documentation, a Notice of Amendment form must be submitted to the Committee (see section 5).
- 2.3 The trial must not commence at any site until the Committee has notified the Chief Investigator that the favourable ethical opinion is extended to the site and management permission or approval has been obtained from the organisation responsible for the care of the participants at the site.
- 2.4 Should the trial not commence within 12 months, the sponsor should give the Committee a written explanation for the delay. It is open to the Committee to allow a further period of 12 months within which the trial must commence.
- 2.5 Should the trial not commence within 24 months, the Committee may review its opinion and may recommend to the MHRA that the CTA should be suspended or terminated.

3. Duration of ethical opinion

- 3.1 The favourable opinion applies for the duration of the trial. If it is proposed to extend the duration of the trial as specified in the application form, the Committee should be notified.
- 3.2 Where the trial involves the use of "relevant material" for the purposes of the Human Tissue Act 2004, authority to hold the material under the terms of the ethical approval applies until the end of the period declared in the application and approved by the Committee.

4. Progress reports

- 4.1 Research Ethics Committees are required to keep a favourable opinion under review in the light of progress reports and any developments in the trial. A progress report should be submitted to the Committee 12 months after the date on which the favourable opinion was given. Annual progress reports should be submitted thereafter until the end of the trial is declared.
- 4.2 Progress reports should be in the format prescribed by NRES and published on the website at <http://www.nres.npsa.nhs.uk/applicants/after-ethical-review/>.
- 4.3 The Committee should be kept informed of any significant findings or recommendations by an independent Data Monitoring Committee or equivalent body established for the trial.

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- 4.4 The Chief Investigator may be requested to attend a meeting of the Committee or Sub-Committee to discuss the progress of the trial.
5. Amendments
- 5.1 If the sponsor proposes to make a substantial amendment to the clinical trial authorisation, the Regulations require that a Notice of Amendment form must be submitted to the Committee and the MHRA. In the case of multi-site studies, there is no requirement to submit notices of amendment to RECs undertaking site-specific assessment (SSA).
- 5.2 A substantial amendment is any amendment to the terms of the request for clinical trial authorisation, or to the terms of the application for ethical review, or to the protocol or other supporting documentation approved by the Committee, that is likely to affect to a significant degree:
- (a) the safety or physical or mental integrity of the trial participants
 - (b) the scientific value of the trial
 - (c) the conduct or management of the trial
 - (d) the quality or safety of any investigational medicinal product used in the trial.
- 5.3 Notices of Amendment should be in the format recommended by the European Commission at Annex 2 to *"Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of a trial"* (ENTR/CT1) and available at <http://eudract.emea.eu.int/document.html#guidance>. The form should be signed by the person submitting the notice.
- 5.4 A substantial amendment on which an ethical opinion has been requested must not be implemented until a favourable ethical opinion has been given by the Committee, unless the changes to the trial are urgent safety measures (see section 7). The Committee is required to give an opinion within 35 days of the date of receiving a valid notice of amendment.
- 5.5 Amendments that are not substantial amendments ("minor amendments") may be made at any time and do not need to be notified to the Committee.
- 5.6 Further guidance on amendments is available at <http://www.nres.npsa.nhs.uk/applicants/after-ethical-review/>.
6. Changes to sites
- 6.1 Where it is proposed to include a new site in the trial, the Site-Specific Information Form (SSI Form) together with the Principal Investigator's CV should be submitted to the relevant REC for site-specific assessment (SSA). If the site was not included in the list of proposed trial sites in the original REC application and request for CTA, a Notice of Amendment form must also be submitted to the Committee under the Regulations. A copy of the Notice of

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Amendment must be sent to the MHRA for information only.

- 6.2 Where it is proposed to make significant changes in the management of a site (in particular, the appointment of a new PI), a Notice of Amendment form must be submitted to the Committee (and to the MHRA for information) *and* a revised SSI Form for the site should be submitted to the relevant REC for SSA, together with the CV for the new PI if applicable.
- 6.3 The Committee should be notified when a site is closed or withdrawn prematurely.
7. Urgent safety measures
- 7.1 The sponsor or the Chief Investigator, or the local Principal Investigator at a trial site, may take appropriate urgent safety measures in order to protect the trial participants against any immediate hazard to their health or safety.
- 7.2 The Regulations require that the Committee and the MHRA must be notified within 3 days that such measures have been taken, the reasons why and the plan for further action.
8. Pharmacovigilance
- 8.1 Safety reporting requirements are set out in "*Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials of medicinal products for human use*" (ENTR/CT3) issued by the European Commission and available at http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/21_susar_rev2_2006_04_11.pdf. Guidance is also available on the NRES website.
- 8.2 Under the Regulations, Suspected Unexpected Serious Adverse Reactions (SUSARs) occurring during the trial in the UK must be notified to the Committee and the MHRA in expedited fashion. A SUSAR which is fatal or life-threatening must be reported as soon as possible and in any event within 7 days after the sponsor became aware of the event. Any additional relevant information must be reported within 8 days of sending the first report. A SUSAR which is *not* fatal or life-threatening must be reported as soon as possible and in any event within 15 days after the sponsor first became aware of the event.
- 8.3 There is no requirement to notify SUSARs occurring in the trial outside the UK or in other trials of the investigational medicinal product (IMP) in an expedited fashion.
- 8.4 There is no requirement to notify serious adverse events occurring in the trial, other than SUSARs.
- 8.5 For each IMP being tested in the trial, the Regulations require the sponsor to provide the Committee and the MHRA with an annual safety report of the safety of the subjects in clinical trials of the IMP for which it is the sponsor (whether in the UK or elsewhere). The report should include an aggregated

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global listing of all Suspected Serious Adverse Reactions (SSARs) occurring in those trials in the reporting period.

- 8.6 Where a commercial sponsor is conducting one or more trials of the IMP outside the UK, it is also requested to provide the Committee with 6 monthly safety reports, including a global line listing of all SUSARs occurring in relevant trials during the reporting period. This is not a requirement of the Regulations.
- 8.7 In the case of double-blinded trials, all reports of adverse reactions must be unblinded.
- 8.8 Pharmacovigilance reports may be provided to the Committee by either the sponsor, or the sponsor's representative, or the Chief Investigator. All submissions should be accompanied by the cover sheet for safety reports published on the NRES website. A single cover sheet may be used for the submission of several reports.
- 8.9 The Chief Investigator and representatives of the sponsor may be requested to attend a meeting of the Committee or Sub-Committee to discuss any concerns about the health or safety of trial participants arising from pharmacovigilance reports.
- 8.10 Reports should not be sent to other RECs in the case of multi-site trials.
9. Conclusion or early termination of the trial
- 9.1 Under the Regulations, the sponsor must notify the Committee and the MHRA in writing that the trial has ended within 90 days of the conclusion of the research. Unless otherwise specified in the protocol, the conclusion of the trial is normally defined as the last visit of the last participant or the completion of any follow-up monitoring and data collection described in the protocol. Any change to the definition of the conclusion of the trial should be notified to the Committee and the MHRA as a substantial amendment.
- 9.2 If the trial is terminated early, the sponsor must notify the Committee within 15 days of the date of termination. An explanation of the reasons for early termination should be given.
- 9.3 Declarations of conclusion or early termination should be on the form issued by the European Commission at Annex 3 to ENTR/CT1 and available at <http://eudract.emea.eu.int/document.html#guidance>.
10. Final report
- 10.1 The sponsor or Chief Investigator should provide the Committee and the MHRA with a summary of the clinical trial report within 12 months of the conclusion of the trial. The Committee should also be notified of the arrangements for publication or dissemination of the research including any feedback to participants.

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11. Review of ethical opinion

- 11.1 The Committee may review its opinion at any time in the light of any relevant information it receives. It has no power to legally withdraw the opinion it has given but may draw the attention of the MHRA to any serious concerns and may recommend that consideration is given to suspending or terminating the CTA.
- 11.2 The sponsor or Chief Investigator may at any time request that the Committee reviews its opinion, or seek advice from the Committee on any ethical issue relating to the trial.

12. Serious breaches of Good Clinical Practice or the protocol

- 12.1 Under the Regulations the sponsor must notify the MHRA of any serious breach of the conditions or principles of Good Clinical Practice (GCP) or of the protocol, within 7 days of the matter coming to its attention. A breach should be regarded as serious if it is likely to affect to a significant degree the safety or physical or mental integrity of the subjects of the trial, or the scientific value of the trial. It is requested that the sponsor should also notify the Committee of such breaches within the same timescale. There is no requirement to notify minor breaches of GCP or the protocol.
- 12.2 A minor deviation from the protocol to deal with unforeseen circumstances is not considered to be a serious breach of the protocol provided that it is approved by the Chief Investigator, either in advance or after the event. However, if the deviation would meet the criteria for a substantial amendment it must be notified to the Committee under the Regulations.
- 12.3 There is no statutory provision for the Committee to approve proposed deviations from the protocol for individual subjects. It is the responsibility of the sponsor to consider whether protocol amendments should be made in such cases. Where the amendment is substantial, it must be notified.

SL-AR1 After ethical review (CTIMPs)
Version 3.3, May 2008

Appendix 2 Clinical trials authorisation: Medicines and Healthcare products Regulatory Agency

MHRA

Safeguarding public health

Dr S Hutchings
CARDIFF UNIVERSITY
SOUTH EAST WALES TRIALS UNIT
7TH FLOOR NEUADD MEIRIONNYDD
HEATH PARK
CARDIFF
CF14 4YS
UNITED KINGDOM

17/03/2011

Dear Dr S Hutchings

THE MEDICINES FOR HUMAN USE (CLINICAL TRIALS) REGULATIONS 2004 S.I. 2004/1031

Our reference: 21323/0029/001-0001
Eudract Number: 2010-023476-23
Product: DURAPHAT DENTAL SUSPENSION 50MG/ML
Protocol number: SPON766-09

NOTICE OF ACCEPTANCE

I am writing to inform you that the Licensing Authority accepts your request for a clinical trial authorisation (CTA), received on 17/02/2011.

The authorisation is effective from the date of this letter although your trial may be suspended or terminated at any time by the Licensing Authority in accordance with regulation 31. You must notify the Licensing Authority within 90 days of the trial ending.

Finally, you are reminded that a favourable opinion from the Ethics Committee is also required before this trial can proceed.


Yours sincerely,

**Clinical Trials Unit
MHRA**

Medicines and Healthcare products Regulatory Agency
151 Buckingham Palace Road London SW1W 9SZ
T 0203 080 6000 www.mhra.gov.uk

An executive agency of the Department of Health

Appendix 3 Cardiff and Vale University Health Board Research and Development letter of approval

	GIG CYMRU NHS WALES	Bwrdd Iechyd Prifysgol Caerdydd a'r Fro Cardiff and Vale University Health Board	Ysbyty Athrofaol Cymru University Hospital of Wales
	Eich cyf/Your ref Ein cyf/Our ref Welsh Health Telephone Network 1872 Direct line/Llinell uniongyrchol	Heath Park, Cardiff, CF14 4XW Phone 029 2074 7747 Fax 029 2074 3838 Minicom 029 2074 3632	Parc Y Mynydd Bychan, Caerdydd, CF14 4XW Ffôn 029 2074 7747 Ffacs 029 2074 3838 Minicom 029 2074 3632

Tel: 029 20746986
 Fax: 029 20745311
 CAV_Research.Development@wales.nhs.uk

From: Professor JI Bisson
 R&D Director
 R&D Office, 2nd Floor TB2
 University Hospital of Wales
 Cardiff
 CF14 4XW

08 April 2011

Dr Ceri Hoddell
 Community Dental Service
 Room 136
 Dental Hospital
 Heath Park
 Cardiff
 CF14 4XY

Dear Dr Hoddell

Re: 11/DEN/5058E : A Randomised Trial To Determine The Relative Cost And Effectiveness Of Pit And Fissure Sealants and Fluoride Varnish in Preventing Dental Decay (Seal or Varnish)

Thank you for your recent communication regarding the above project, which was reviewed on 25 March 2011 by the Cardiff and Vale Research Review Service (CaRRS).


Documents submitted for review were:

Document	Version	Date
Favourable Opinion Letter from Research Ethics Committee		15 February 2011
NHS RD Form	3.1	Received 4 March 2011
SSI Form	3.1	Received 4 March 2011
Protocol and supporting documentation	1.0	11 January 2011
Information Sheet: Parent	1.0	12 January 2011
Information Sheet: Child	1.0	12 January 2011
Patient Consent Form	1.0	12 January 2011
Medical History Form	1.0	12 January 2011
GP Letter of Invitation	1.0	12 January 2011
Invitation Letter for Pare/Guardian	1.1	11 February 2011

Version 1.0. 30.06.10
 Letter 2a

Page 1 of 2

Bwrdd Iechyd Prifysgol Caerdydd a'r Fro yw enw gweithredol Bwrdd Iechyd Lleol Prifysgol Caerdydd a'r Fro
 Cardiff and Vale University Health Board is the operational name of Cardiff and Vale University Local Health Board


 UHW129X

I am pleased to inform you that the Panel has no objection to your proposal.

R&D approval from Cardiff and Vale UHB is now subject to:

- Receipt of an approved study agreement signed by all parties
- Receipt of a signed copy of the document "Standard Conditions of Management Approval for Clinical Trials of Investigational Medicinal Products"

Once the above are in place, an R&D approval letter will be issued. You should not begin your project before receiving this written confirmation from the R&D Office.

If you require any further information or assistance, please do not hesitate to contact staff in the R&D Office.

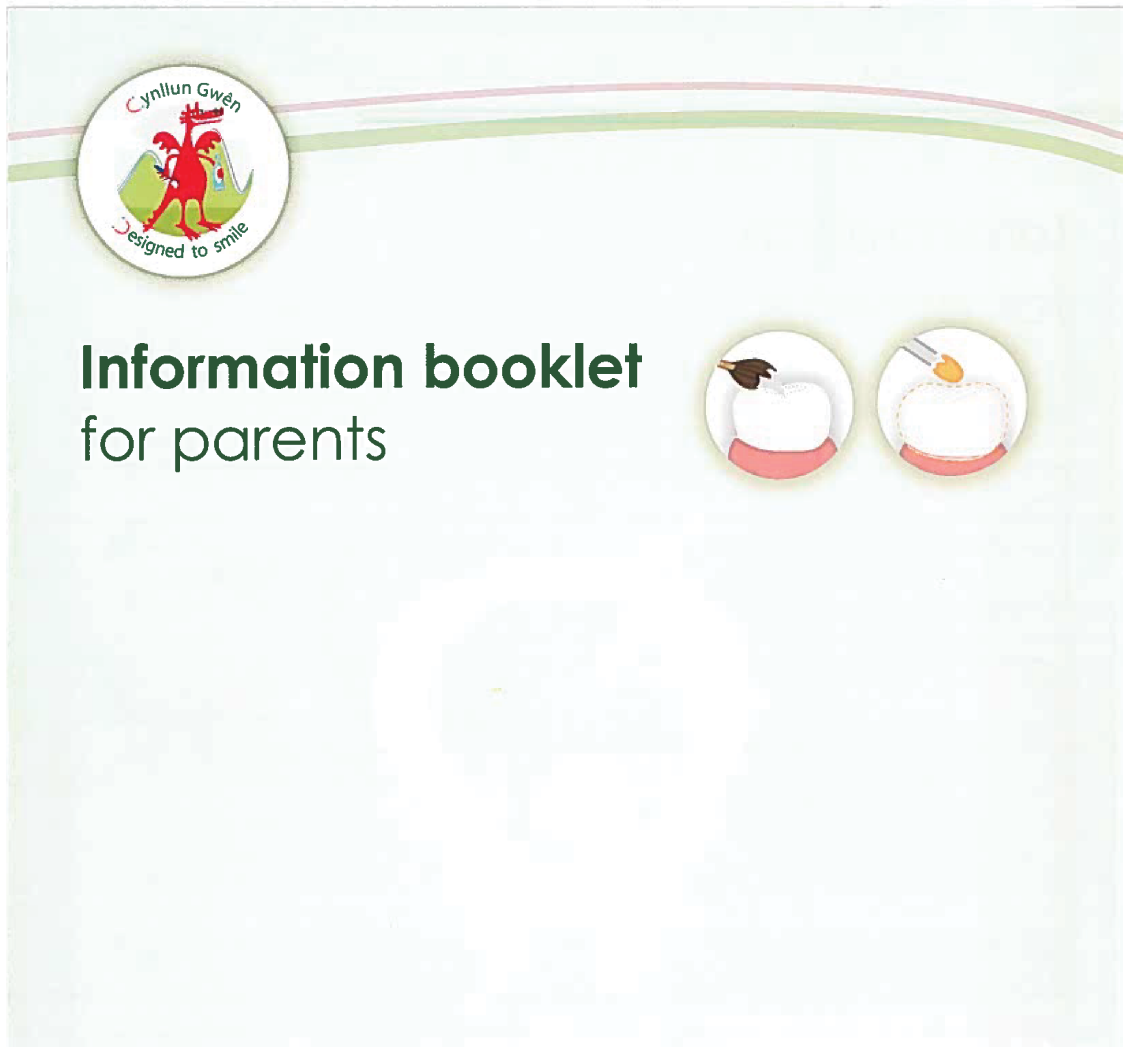
Yours sincerely,



Professor Jonathan I Bisson
Chair of the Cardiff and Vale Research Review Service (CaRRS)

CC Prof Barbara Chadwick, R&D Lead
Sponsor contact, Chris Shaw
Kathryn Bethune, Clinical Trials Pharmacist
Anthony Williams, Finance
Trial Manager, Simon Hutchings

Appendix 4 Participant information sheet for parents (version 2.1)



**Information booklet
for parents**




Dear Parent/Guardian,


The Cardiff and Vale Community Dental Service would like to invite you and your child to help us evaluate two dental treatments to find out which one works best.

Before you decide if you want you and your child to take part or not, you need to know why the evaluation (study) is being done and what it will involve.

Please take the time to read the following information carefully. If you have any questions or want to know more, please call this number:

02920 687624




 Bwrdd Iechyd Prifysgol
Caerdydd a'r Ffr
Cardiff and Vale
University Health Board


**SEAL OR
VARNISH**

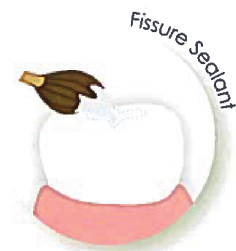
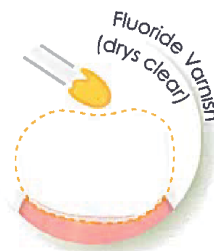
Information for parents

Q & A



What is this study about?

Dentists use two treatments to help prevent tooth decay in children's adult molar (back) teeth. One is a fluoride 'varnish' which is painted on to the tooth (like fluoride toothpaste only stronger) that helps strengthen the tooth against decay. The second is a plastic coating (or 'sealant') to prevent the harmful bacteria that cause tooth decay collecting on the tooth surface.



- Both treatments have been shown to work, and have been used for many years. We would like to find out if one treatment is better than the other, because no one currently knows.
- We also want to know what children, parents and the school think about the two treatments.
- We need the help of 920 Year 2 primary children (and their parents) to successfully complete the evaluation, which will last 3 years.

Why have my child and I been invited?

Because your child's school has been chosen and agreed to take part in this study.



Do my child and I have to take part?

No. It is totally up to you. If you choose for your child not to take part in the study, your child will still be able to take part in the existing Community Dental Service programme for prevention of tooth decay (See 2 & 7 on the CONSENT FORM).



What are the possible disadvantages and risks of taking part?

There are no significant disadvantages or risks for you or your child if you take part in the study.

What are the possible advantages about taking part?

There are unlikely to be any direct benefits for you or your child from taking part in the study, over and above the benefits of taking part in the current 'Designed to Smile' Fissure Sealant Programme. However both you and your child will be contributing to our understanding of which of the two treatments (fluoride varnish or plastic sealant) works best.

Will my taking part be kept confidential?

If you and your child choose to participate we would like to tell your child's dentist, but only with your permission (See 3 on the CONSENT FORM).

All information collected about you and your child during the course of the study will be kept strictly confidential (see 4 & 5 on the CONSENT FORM).

What if I do not want my child or I to carry on being part of the study?

You can decide for you and your child to stop taking part at any time during the study, without giving a reason, by phoning **02920 687624**. If you decide to stop taking part, your child's dental care and the legal rights of either you or your child will not be affected in any way.

In order for us to understand the reasons why parents withdraw their children from the study, if you withdraw your child for any reason, with your permission (See 8 on the CONSENT FORM) we would like to contact you to find out why.





What will happen to the results of the research study?

- At the end of the study the results will be published in medical/dental journals and presented at dental conferences. Information that relates directly you or your child **will not** be presented.
- We will also give you and your child's school a summary of the findings from this study. You or your child **will not** be identified in any summary or report.



Who has funded and approved the study?

- This study has been funded by the Department of Health, and is being managed by Cardiff University in collaboration with the Community Dental Service.
- It has been looked at and approved by the independent Research Ethics Committee for Wales. Their job is to protect your safety, rights, wellbeing and dignity. The study has also been reviewed and approved by the UK medicines regulatory authorities.
- We have also received help and advice from the Forest Parents Group at the Forest Children's Centre, Dulfryn, Newport (<http://www.forestchildrenscentre.org.php>), to present the information provided to you in an understandable and jargon-free way.



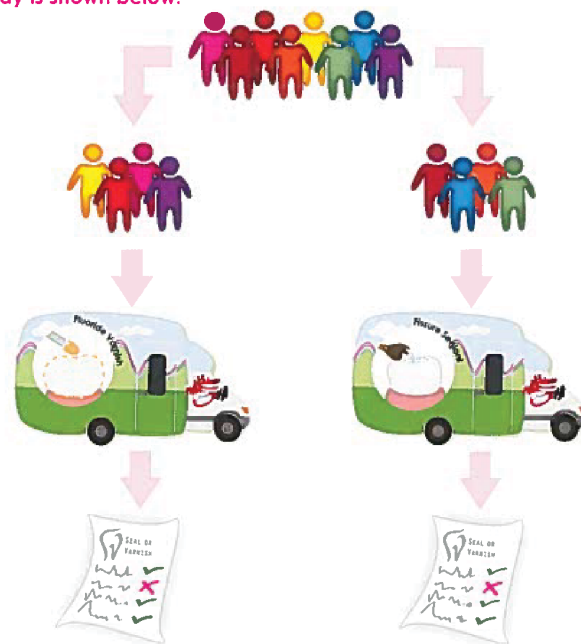
What if there is a problem?

- If at any point you are unhappy with any aspect of you or your child's involvement in the study, please advise the Dental Team (02920 336414 or 07974 372002). If you remain unhappy and wish to formally complain, you can do this through the normal NHS complaints procedure.
- In the event that something does go wrong and your child is harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against Cardiff & Vale University Health Board Cardiff University Health Board and/or Cardiff University but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

What will happen to my child and I if we take part?

- The Mobile Dental Clinic will visit your child's school early in the school year to look at your child's teeth to see if they are suitable for the study. The dentist will let you know if there are any problems with your child's teeth that need treatment.
- If your child is suitable for the study, he/she will receive either fluoride varnish or plastic sealant. Which treatment your child receives will be chosen randomly (by chance) using a computer. Your child will have a 50/50 chance of receiving either treatment.
- Your child will then be seen by the dental team and receive treatment (when required) every 6 months for the next 3 years through the Mobile Dental Clinic.

A summary of the study is shown below:



- After being seen by the dental team your child will be asked some questions about how they felt about the treatment.
- At the start and then each year we will be asking you to complete a short questionnaire relating to your child's dental health.
- At the beginning and end of the study a small number of children (in pairs) will be invited to speak with a member of the study team at the school to help us understand in more detail how children felt about the treatment they received. These sessions may be recorded (audio only), but only if you give your permission.
- We would also like to contact a number of parents by telephone at the beginning and at end of the study to hear their thoughts and feedback about the treatment their children received and on taking part in the study (the telephone call may also be recorded, but only if you give your permission).

What do I need to do now?

- We would like you to talk about the study with your child to help decide if you would both like to take part.
- If you decide you would both like to take part, please complete the following, and give to your child to hand in at school using the enclosed envelope:

1) MEDICAL HISTORY FORM

The Medical History Form includes sections for patient details, medical history, and dental history. It features a red dragon logo and the text 'Synlun Gwên designed to smile' and 'SEAL OR VARNISH'.

2) CONSENT FORM

(please remember to sign and date)

The Informed Consent Form contains detailed information about the study, including the purpose, procedures, risks, and benefits. It includes a red dragon logo and the text 'Synlun Gwên designed to smile' and 'SEAL OR VARNISH'.

- If your child normally sees your family dentist (for check-up etc) they should continue to do so during the study.
- During the study if you need to speak to a member of the dental team please call **02920 336414** or **07974 372002**.

Thank you for considering taking part in this study



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v2.1/24May2011



Appendix 5 Medical history form (version 1.1)






Medical History Form

(To be completed by person with parental responsibility)

Please complete this form providing as much detail as possible. If you are unsure about any of the questions please contact a member of the dental team using the telephone number below.

Call 02920 687624 for more information

Name of Primary School _____

Class Name/Number _____

Child's Full Name _____

Home Address _____

Postcode _____

Daytime Tel. _____

Child's Date of Birth ____/____/____
Day/Month/Year

Does your child have any allergies? Yes No

If yes what is he/she allergic to? _____

Has your child ever been admitted to hospital **overnight** (i.e. to a bed in a ward) due to:

Allergies? Yes No

Asthma? Yes No

Is your child currently taking part in another clinical trial? Yes No

If yes, please give details: _____

For Community Dental Service use only:

Scheduled for baseline examination? Yes No Planned date of examination:


Received by SEWTU: Received by (initials):

Entered into database: Entered by (initials):


SID: PID:

V1.1 - 24May2011
© Artwork Cardiff University


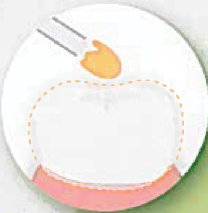
Appendix 6 Informed consent form (version 2.1)




Cynllun Gwên
Designed to smile




**SEAL OR
VARNISH**



**GIG
NHS
Wales**

Bwrdd Iechyd Prifysgol
Caerdydd a'r Fro
Cardiff and Vale
University Health Board



**CARDIFF
UNIVERSITY
PRIFYSGOL
CARDIFF**

**Call 02920 687624
for more information**

Informed Consent Form

(To be completed by person with parental responsibility)

Title of Study:
Seal or Varnish? A Randomised Study To Determine The Relative Cost And Effectiveness Of Pit And Fissure Sealants And Fluoride Varnish In Preventing Dental Decay.

Tick box:

1. I confirm that I have read and understand the information sheet (version 2.1, dated 24 May 2011) for the above study and have had the opportunity to ask questions by telephone with a member of the dental team.

2. I understand that my participation and that of my child is voluntary and that I and my child are free to withdraw at any time, without giving any reason, without our medical care or legal rights being affected.

3. I agree to my child's dentist being informed about his/her participation in the study.

If your child is not registered with a dentist please tick here

4. I understand that relevant sections of my child's notes and the data collected during the study may be looked at by members of the South East Wales Trials Unit (SEWTU), and by the UK medicines regulatory authorities to check that the study is being carried out properly. I give permission for these individuals to have access to my child's records for this purpose.

5. I understand that information about me and my child (including names and address) will be held at SEWTU according to the 1998 Data Protection Act. I understand that this information will be kept strictly confidential and that no personal information will be used in the study report or other publications.

6. I agree to take part in the above Study and I also agree for my child to take part in the above study.

7. I agree for my child to participate in the existing 'Designed to Smile' Fissure Sealant programme if the dental team finds that my child is not suitable for participation in the Seal or Varnish study.

8. I understand that I may withdraw my child and I from the study at any time, for any reason. If my child and I withdraw... (please tick which applies)

I agree

I do not agree

...for a member of the trial team to contact me to try and understand the reasons for withdrawing.

Name of child _____

Child's Date of Birth ____/____/____

Name of person with parental responsibility _____

Signature of person with parental responsibility _____

Date ____/____/____

For Community Dental Service use only:

SID: PID:

P.w./P.C. verified? (initial and date)

v2.1/24May2011
Artwork, Cardiff University

Appendix 7 Medical history follow-up form (version 1.2)



ynllun Gwên
Designed to smile

Seal or Varnish Medical History Update Form

Dear Parent/Guardian,

You have previously agreed for your child to take part in the Seal or Varnish study, which is evaluating two different ways of protecting children's teeth from tooth decay.

In order for the dental team to make sure your child is still suitable to take part in the study, we need you to let us know if there has been any significant change in your child's health in the last year.

If the answer is **YES** to any of the questions on the form, please complete the form and return it to the study team in the enclosed envelope.

If there has been **no change** to your child's health in the last year you **DO NOT** need to return the form.



SEAL OR VARNISH





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Caerdydd a'r Fro
Cardiff and Vale
University Health Board



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UNIVERSITY

Call 02920 687624
for more information

(To be completed by person with parental responsibility)

Child's Full Name:

Child's Date of Birth:/...../.....
Day Month Year

Does your child have any allergies? Yes No

If yes what is he/she allergic to?
.....
.....

Has your child ever admitted to hospital overnight (i.e. to a bed in a ward) due to:

Allergies? Yes No

Asthma? Yes No

Is your child currently taking part in another clinical trial? Yes No

If yes, please give details:
.....
.....

Name of person with parental responsibility:

Signature of person with parental responsibility:

Date:/...../.....
Day Month Year

For Community Dental Service use only:

Received by SEWTU: Received by (initials):

Entered into database: Entered by (initials):

SID: PID:

Version 1.1 - 08Sep2011
Artwork Cardiff University

Appendix 8 Cardiff and Vale University Health Board Community Dental Service clinical protocol for application of Delton® Pit and Fissure Sealant



It is necessary to remove plaque and debris from the enamel and the pits and fissures of the tooth. Any debris that is not removed will interfere with the proper etching process and the sealant penetration into the fissures and pits. Children who are to have fissure sealant applied should brush their teeth / have their teeth brushed with a toothbrush beforehand.

Risk Assessment

This risk assessment reduces the possibility of children with oral/ facial infections being included.

The risk assessment is carried out **BEFORE** the application procedure is started. This is to ensure that any child with any abnormality of the lips, face or soft tissues of the mouth is excluded. Children who are showing obvious signs of systemic illness e.g. colds, 'flu, chicken pox etc should also be excluded on that day.

The Risk Assessment should be carried out as follows:

The Extra-Oral Assessment

- Check the skin of the face and around the mouth for abnormalities (spots, inflammation, swelling etc)
- Check the lips for lesions/ infections

The Intra-Oral Assessment

- Check the right and left inner cheeks and the insides of the lips using the disposable mirror provided in the pack
- Check the top and underneath the tongue.

The teeth and gums should be checked for signs of decay and/ or infection in the following order:

- Check the upper right teeth and gums
- Check the upper left teeth and gums
- Check the lower right teeth and gums
- Check the lower left teeth and gums

If everything appears normal the fissure sealant may be applied. Children with abnormalities of the skin around the mouth, lips (e.g. cold sores), or soft tissue lesions should not have the fissure sealant applied.

If the child has any abnormality of the lips or mouth, they should be referred for a dental opinion.

The Application Procedure

Once the risk assessment has been carried out, the application procedure can begin. If a child gets upset or protests during any part of the procedure, the procedure should be abandoned.

Step 1: Isolate the tooth/teeth

- It is absolutely imperative to keep the tooth free from salivary contamination
- Use dry guards, cotton wool rolls or saliva ejectors to aid moisture control

Step 2: Dry the surfaces

Step 3: Etch the surfaces

- The etchant should be applied to all the pits and fissures. In addition, it should be applied at least a few millimeters beyond the final margin of the sealant and in accordance with manufacturer directions
- Do not allow the etchant to come into contact with the soft tissue. If this occurs, rinse the soft tissue thoroughly

Step 4: Rinse and dry the tooth/teeth

- Rinse all the etchant material from the tooth in accordance with manufacturer directions
- The tooth is dried until it has a chalky, frosted appearance. If it does not, the tooth should be re-etched in accordance with manufacturer directions. It is

imperative to avoid salivary contamination. There is agreement that moisture contamination at this stage of the process is the most common cause of sealant failure

Step 5: Apply the material and evaluate for voids, marginal discrepancies or retention problems

- Be careful not to incorporate air bubbles in the material
- Follow protocol for light cured dental sealant material in accordance with manufacturer directions
- After the sealant has set, the operator should wipe the sealed surface with a wet cotton pellet. This allows for the removal of the air-inhibited layer of the non-polymerized resin. Failure to perform this step may leave an objectionable taste in the child's mouth

Step 6: Evaluate the sealant

- The sealant should be evaluated visually and tactically. Attempt to dislodge it with a probe
- If there are any deficiencies in the material, more sealant material should be applied

Step 7: Evaluate the occlusion

- Unfilled resins will wear down naturally and do not require occlusal adjustment

Step 8: End of Procedure

- Reward child with a motivation sticker

Appendix 9 Duraphat[®] summary of product characteristics

1. NAME OF THE MEDICINAL PRODUCT

Duraphat 50 mg/ml Dental Suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of suspension contains 50 mg Sodium Fluoride equivalent to 22.6 mg of Fluoride

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dental Suspension

Brown/yellow, opaque suspension

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the prevention of caries in children and adults as part of a comprehensive control programme.

For the:

- prevention of recurring (or marginal) caries
- prevention of progression of caries
- prevention of decalcification around orthodontic appliances
- prevention of pit and fissure (occlusal) caries.

For the desensitisation of hypersensitive teeth as part of a treatment regimen which includes the daily use of a suitable toothpaste.

4.2 Dosology and method of administration

Duraphat 50 mg/ml Dental Suspension is to be applied by the dentist. Before applying Duraphat, excess plaque should be removed and the teeth dried.

Duraphat is applied as a thin layer to the most susceptible areas of dentition using a brush, probe or swab.

Recommended dosage for single application:

For milk teeth: up to 0.25 ml (=5.65 mg Fluoride)

For mixed dentition: up to 0.40 ml (=9.04 mg Fluoride)

For permanent dentition: up to 0.75 ml (=16.95 mg Fluoride)

For caries prophylaxis, the application is usually repeated every 6 months but more frequent applications (every 3 months) may be made.

For hypersensitivity, 2 or 3 applications should be made within a few days.

The patient should not brush the teeth or chew food for 4 hours after treatment.

Method of administration: For dental use

4.3 Contraindications

Hypersensitivity to colophony and/or any other constituents.

Ulcerative gingivitis.

Stomatitis.

Bronchial asthma.

4.4 Special warnings and precautions for use

Application of Duraphat 50 mg/ml Dental Suspension to the whole dentition should not be carried out on an empty stomach.

On the day when Duraphat has been applied, no high dose Fluoride preparations, such as Fluoride gels, should be used. The administration of Fluoride supplements should be suspended for several days after applying Duraphat.

4.5 Interaction with other medicinal products and other forms of interaction

The presence of alcohol in the Duraphat formula should be considered.

4.6 Pregnancy and lactation

As this product contains 33.8% of ethanol (each dose contains up to 0.2 g of alcohol), it is recommended to avoid its use in pregnant women and during lactation.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Gastrointestinal disorders:

Very rare (<1/10,000): Stomatitis, gingivitis ulcerative, retching, oedema mouth and nausea may occur in sensitive (allergic) individuals - if necessary, the dental suspension layer can easily be removed from the mouth by brushing and rinsing.

Skin and subcutaneous tissue disorders:

Very rare (<1/10,000): Irritation in sensitive individuals, angioedema

Respiratory, thoracic and mediastinal disorders:

Very rare/Isolated report (<1/10,000): Asthma

4.9 Overdose

In very high doses, Fluoride has an acute toxic action through inhibition of enzymes resulting in hypocalcaemia. Doses of several milligrams of Fluoride per kg body weight may cause nausea and vomiting, and diarrhoea.

Tetany and convulsions can occur, as well as cardiovascular disorders.

The dental suspension layer can easily be removed from the mouth by brushing and rinsing.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotheapeutic group: Stomatological preparations, caries prophylactic agents

ATC code: A01A A01

Sodium Fluoride applied topically after tooth eruption reduces caries by inhibiting demineralisation and promoting remineralisation of the tooth surface and by inhibiting the cariogenic microbial process.

Duraphat 50 mg/ml Dental Suspension also reduces dentinal hypersensitivity.

In the management of dental erosion associated with the frequent consumption of acidic beverages or gastric reflux, high concentration topical Fluoride agents are considered to be of value. Duraphat is at least as effective as 2% Sodium Fluoride Solution in inhibiting erosion *in vitro*

5.2 Pharmacokinetic properties

After oral administration, Fluoride absorption is rapid and extensive (90-100%) with peak Fluoride plasma levels reached within 30 to 60 minutes after ingestion. Fluoride is widely distributed through the body and concentrates in

bone and teeth. About 50% of Fluoride is stored. Excretion is primarily through the kidneys with less than 10% being excreted in the faeces and less than 1% in sweat and saliva.

Duraphat covers teeth with a film of suspension which hardens in the presence of saliva and then persists, and which over the following hours causes Fluoride to accumulate at a measurable depth in the tooth enamel.

5.3 Preclinical safety data

The product is used under total control of the dentist and the amount of Fluoride introduced to the patient at one time is within acceptable safety limits. The recommended doses are up to 0.75 ml for permanent dentition. Treatment is recommended every 6 months or a maximum of every three months. For hypersensitivity 2-3 applications are recommended within a few days. These levels of Fluoride introduced are again within acceptable safety limits.

Due to the slow release of Fluoride, the plasma levels are even lower than levels known to produce no side effects in children.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol 96%

White Wax (E901)

Shellac (E904)

Colophony

Mastic

Saccharin (E954)

Raspberry Essence (containing Ethyl Butyrate, Geraniol, Iris Resinoid, Isoamyl Acetate, Jasmine Absolute, Vanillin and Propylene Glycol).

6.2 Incompatibilities

None known

6.3 Shelf life

Unopened 3 years. For aluminium tube: after opening, use within 3 months.

6.4 Special precautions for storage

Do not store above 25°C

6.5 Nature and contents of container

Boxes of 1 x 10 ml or 5 x 30 ml tubes made of internally lacquer-coated aluminium, externally printed, with white plastic screw cap with sealing plug.

Boxes of 1 x 1.6 ml or 5 x 1.6 ml glass cylinders with a cream bromobutyl rubber stopper and gold aluminium cap at the top and dark blue chlorobutyl rubber stopper at the bottom.

6.6 Instruction for Use/Handling

If necessary the teeth should be cleaned, especially at the sites most susceptible to caries. When groups of patients (e.g. children) are to be treated, they should clean the teeth themselves using a toothbrush.

To start, clear one or two quadrants of excessive saliva using an air syringe (or dabbing with cellulose). Duraphat 50 mg/ml Dental Suspension is applied from the tube using a miniature cotton swab, probe or brush, painting and dabbing repeatedly to form a thin layer. Then treat the next quadrants in the same manner. It is advisable to begin by applying the dental suspension to teeth in the

lower jaw before too much saliva collects and interferes. It may not be necessary to paint the lingual surfaces since these are generally more caries-resistant; Duraphat should preferably be applied to those spots most susceptible to caries attack.

Application of Duraphat from the cylinder is particularly suited to targeted, low-dose application. A blunt cannula is used with the end bent to an angle to facilitate application to approximal and distal surfaces. For application to approximal surfaces place the cannula between adjacent teeth and deliver a small amount of Duraphat. The dental suspension should be applied from both sides of the interproximal space and occlusally.

For fissures, a drop of Duraphat should be spread along the fissure using the cannula. Edges of fillings and crowns and hypersensitive tooth necks can be treated in the same way.

The smooth surfaces of the teeth should be treated when caries activity is high, particularly if decalcification is evident. The cannula should be placed tangentially to the teeth and Duraphat distributed with the side of the curved cannula end.

Areas around fixed orthodontic devices can be treated with Duraphat using the cannula.

The yellowish colour of Duraphat facilitates its application and control.

Duraphat sets in the presence of saliva. The effect of Duraphat depends upon the prolonged activity of the Fluoride. The dental suspension film should not be removed prematurely. Patients should be advised not to brush their teeth or chew food for at least 4 hours after treatment; during this time, soft foods and liquids may be consumed. However, if you need to, the dental suspension layer can easily be removed by brushing or rinsing.

Instruments, clothing, etc. which comes into contact with Duraphat can be cleaned with alcohol.

7. MARKETING AUTHORISATION HOLDER

Colgate-Palmolive (UK) Limited

Guildford Business Park

Middleton Road

Guildford

Surrey

GU2 8JZ

8. MARKETING AUTHORISATION NUMBER(S)

PL 0049/0042

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

First Authorisation: 06/03/1998

Renewals: 06/03/2008 and 15/07/2008

10. DATE OF REVISION OF THE TEXT

10 February 2012

Appendix 10 Cardiff and Vale University Health Board Community Dental Service clinical protocol for application of Duraphat® fluoride varnish



Risk Assessment

This risk assessment reduces the possibility of children with oral/ facial infections being included.

The risk assessment is carried out **BEFORE** the application procedure is started. This is to ensure that any child with any abnormality of the lips, face or soft tissues of the mouth is excluded. Children who are showing obvious signs of systemic illness e.g. colds, 'flu, chicken pox etc should also be excluded on that day.

The Risk Assessment should be carried out as follows:

The Extra-Oral Assessment

- Check the skin of the face and around the mouth for abnormalities (spots, inflammation, swelling etc)
- Check the lips for lesions/ infections

The Intra-Oral Assessment

- Check the right and left inner cheeks and the insides of the lips using the disposable mirror provided in the pack
- Check the top and underneath the tongue.

The teeth and gums should be checked for signs of decay and/ or infection in the following order:

- Check the upper right teeth and gums
- Check the upper left teeth and gums
- Check the lower right teeth and gums
- Check the lower left teeth and gums

If everything appears normal the varnish may be applied. Children with abnormalities of the skin around the mouth, lips (e.g. cold sores), or soft tissue lesions should not have the varnish applied.

If the child has any abnormality of the lips or mouth, they should be referred for a dental opinion.

Safety

Children should not take fluoride supplements on the day before, of or following varnish application.

There should be no opportunity for child to ingest more than a single dose.

In the mixed dentition, the recommended dose is 0.4ml.

Acute fluoride toxicity causes nausea and vomiting. If suspected, give milk to drink and arrange for immediate transfer to A&E.

The Application Procedure

- 1 The teeth should be 'toothbrush' clean prior to application of varnish
- 2 Gently retract the cheek using a finger or disposable mirror
- 3 Dry the tooth to be treated using a cotton wool roll
- 4 Place the cotton wool roll in the buccal sulcus
- 5 Apply a thin layer of varnish to pits, fissures and smooth surfaces of first permanent molars using a disposable microbrush
- 6 Remove cotton wool roll
- 7 Repeat in all remaining quadrants
- 8 Advise the child not to eat or drink for 30 minutes and not to brush their teeth for 4 hours after application
- 9 Reward child with a motivation sticker

Appendix 11 International Caries Detection and Assessment System training and calibration protocol

A. Summary

This protocol describes the training and calibration of dental examiners who will undertake clinical assessments as part of the Seal or Varnish Clinical Trial. These examiners will be experienced Community Dental Officers, employed by Cardiff and Vale University Health Board with substantial clinical experience of the examination of young children. A Training and Calibration exercise will be undertaken on four occasions during the study at baseline before the baseline clinical assessment and at 12, 24 and 36 months ahead of the caries assessments.

B. Aim

To train two dentists involved in the caries assessment to use the ICDAS caries assessment.

C. Training of dental examiners

- The Training and Calibration will be based on British Association for the Study of Community Dentistry (BASCD) Training and Calibration Guidance⁽⁷⁴⁾ with substitution of the International Caries Detection & Assessment System (ICDAS).⁽⁷⁵⁾
- Training will involve an online International Caries Detection & Assessment System (ICDAS)⁽²⁶⁾ training package and a training day. Examiners and recorders will be given access to the training package ahead of the training day to give them the opportunity to familiarise themselves with all aspects of the criteria and conventions prior to the start of the training day. The training day will be led by Professor Christopher Deery (University of Sheffield) an experienced ICDAS examiner. It will involve a seminar to review the criteria followed by caries assessments of twenty 6-7 year old primary school children from a Community First school in South Wales to practice use of the criteria. A formal Calibration carried out on ten different children will be undertaken after the practice examinations.

D. Recruitment of children for training purposes

- Recruitment of children for the training exercise will take place in a Community First school in South Wales once agreement has been obtained from the head

teacher. A letter to head teachers is included (Section M). The school used for the Training and Calibration exercise will not be used in the main study.

- Written consent will be obtained for the children to be examined as part of the training course. A letter will be sent (via the school) to the parents of children aged 6-7 years and positive consent obtained for them to take part. A letter / consent form for parents is attached (Section L).
- Sufficient children (30-35) will be recruited for the training session to ensure that they are not examined continuously. If any child does not wish to participate on the day or becomes tired, another will be substituted.

E. Conduct of Dental Examination

- Dental examinations will be conducted within the schools using conventional dental epidemiological survey techniques in line with British Association for the Study of Community Dentistry -co-ordinated surveys.⁽⁷⁴⁾
- The examiner will be seated behind the subject who will be in a supine position on a table or reclined sun-lounger.
- Children will be given a new, sterile toothbrush of appropriate size and asked to brush their teeth. No toothpaste will be used and the toothbrush will immediately be discarded and treated as clinical waste. This aspect of the examination is necessary to allow visualisation of the tooth surfaces to record dental caries in its earliest stages (enamel caries). In the event that plaque or food debris remains adherent, supragingival deposits will be removed by the dentist using either a toothbrush or probe.

F. The examination equipment

- A purpose built light yielding 4000 lux at 1 metre (e.g. Daray) or a similar protected light source will be used for illumination.
- Extension flex and plug adapter for use when necessary with the lamp.
- Disposable paper roll for laying out instruments.
- Materials to ensure cross-infection control including containers for clean instruments, containers for dirty instruments, disinfectant spray/wipes, clean latex-free gloves, eye protection for subjects, clinical waste bags together with sufficient cotton wool buds/rolls etc. for each child.

- Examiners will wear a fresh pair of gloves for each examination.
- Diagnoses will be visual using a plane mouth mirror. A blunt ball-ended probe (CIPTN) with an end diameter of 0.5mm will be used as described below.
- All necessary steps must be taken to prevent cross-infection. A fresh set of previously sterilised instruments will be used for each subject.

G. Examination procedure

- Data will be recorded onto a paper chart chairside.
- Teeth will be examined for caries in the following order:
 - (a) Upper Left to Upper Right
 - (b) Lower Right to Lower Left
- Surfaces will be examined in the following order:-
 - Distal, Occlusal, Mesial, Buccal, Lingual
- Each tooth will be identified and each surface recorded according to the diagnostic criteria for caries.
- Presence or absence of sepsis in the mouth will be noted and coded.
- If a primary tooth is missing, the state of the permanent successor will be recorded. In cases where both the primary tooth and its permanent successor are present further details will be recorded for the permanent tooth only.
- A tooth is deemed to be present if any part of it is visible.

H. Caries Criteria (ICDAS)

- The ICDAS detection codes for coronal caries range from 0 to 6 depending on the severity of the lesion. There are minor variations between the visual signs associated with each code depending on a number of factors including the surface characteristics (pits and fissures versus free smooth surfaces), whether there are adjacent teeth present (mesial and distal surfaces) and whether or not the caries is associated with a restoration or sealant. Therefore, a detailed description of each of the codes is given under the following headings to assist in the training of examiners in the use of ICDAS: Pits and fissures; smooth surface (mesial or distal); free smooth surfaces and caries associated with restorations and sealants (CARS). However, the basis of the codes is essentially the same throughout:

Code	Description
0	Sound
1	First Visual Change in Enamel (seen only after prolonged air drying or restricted to within the confines of a pit or fissure)
2	Distinct Visual Change in Enamel
3	Localized Enamel Breakdown (without clinical visual signs of dentinal involvement)
4	Underlying Dark Shadow from Dentin
5	Distinct Cavity with Visible Dentin
6	Extensive Distinct Cavity with Visible Dentin

- ICDAS two-digit coding method. A two-number coding system is suggested to identify restorations/sealants with the first digit, followed by the appropriate caries code, for example a tooth restored with amalgam which also exhibited an extensive distinct cavity with visible dentin would be coded 4 (for an amalgam restoration) 6 (distinct cavity), an unrestored tooth with a distinct cavity would be 06. The suggested restoration/sealant coding system is as follows:

0 = Sound: i.e. surface not restored or sealed (use with the codes for primary caries)

1 = Sealant, partial

2 = Sealant, full

3 = Tooth colored restoration

4 = Amalgam restoration

5 = Stainless steel crown

6 = Porcelain or gold or PFM crown or veneer

7 = Lost or broken restoration

8 = Temporary restoration

9 = Used for the following conditions

96 = Tooth surface cannot be examined: surface excluded

97 = Tooth missing because of caries (tooth surfaces will be coded 97)

98 = Tooth missing for reasons other than caries (all tooth surfaces will be coded 98)

99 = Unerupted (tooth surfaces coded 99)

I. Procedure in the event of serious pathology being suspected

- In the course of the training or calibration, an examining dentist may encounter suspected serious pathology (e.g. malignancy). This is very unlikely as the prevalence of such potentially serious pathology is extremely low in this age group. The examination is not a screening exercise and does not involve examination of the oral soft tissues. However, it is possible that such a lesion may be noticed and, as the implications are serious, a protocol to deal with this eventuality is in place.
- In the event that such a lesion is noted, the examiner is obliged to follow a set protocol, which is designed to make sure that the participant's parent or carer is informed, whilst not causing unnecessary worry or alarm.
- The examiner will note the child's name, date of birth and school and will contact one of the survey consultants by telephone, a Consultant in Paediatric Dentistry (Professor Barbara Chadwick). The Consultant will liaise with the examining clinician to obtain parental / carers contact details. Parents will then be contacted by telephone and arrangements made for the child to be seen by their general medical practitioner. A follow-up letter will be sent to the parents/carers and the child's medical practitioner.

J. Data analysis

- A master sheet will be completed for each training session to allow comparison between examiners at the tooth or surface level.
- The number of decayed missing and filled teeth or surfaces each examiner has recorded when examining the same child will be compared to and differences highlighted and discussed.
- For training, no formal statistical analyses will be undertaken and discussions use differences identified from the master sheets and individual charts for instant feedback.
- For calibration ten children will be examined and data entered onto a master sheet.
- Calculation of mean indices (DMFT,FT,dmft,dt) by examiner and the size and direction of the deviation from the benchmark examiner will be compared.
- Subsequently inter and extra examiner agreement will be determined using Kappa statistics.

Appendix 12 Delighted–Terrible Faces scale



QDT:SoV Delighted - Terrible Faces Scale (DENTAL TEAM)

School ID:

Participant ID:

Initials:

Date of Birth (dd/mm/yyyy):

/ /

Gender:

Male Female

Visit:

Baseline 18 month

6 month 24 month

12 month 30 month

Assistance to complete form
provided?

Yes No

Date form completed (dd/mm/yyyy):

/ /

**This side (page 1) of the form
should be completed by a
member of the Dental Team.**

**The CHILD should complete
the scale on the other side
(page 2) immediately after
receiving treatment.**

SEWTU USE ONLY

SoV Delighted-Terrible faces Questionnaire
(v1.0 29Jul2011)

Date received by SEWTU: / /

Received by (initials):

Date entered on database: / /

Entered by (initials):

SoV Delighted-Terrible faces Questionnaire (v1.0 29Jul2011)

How did you feel during the treatment?



If you had to have the treatment tomorrow, how would you feel?



How do you feel about the time it took to have the treatment?




How do you feel about the taste of the treatment?




How much did you feel like being sick during the treatment?



Appendix 13 Dental health questionnaire (version 2.2)



Cynllun Gwên
Designed to smile



**SEAL OR
VARNISH**

For office use only

School ID: Participant ID: Timepoint: Baseline 12 mo 24 mo 36 mo

Seal or Varnish Study - Dental Health Questionnaire

Dear Parent,

Please answer the following questions relating to your child's dental health. The questionnaire is split in to 2 parts: Part A relates to your child's normal dental routine and Part B relates to how much of your time is taken up looking after your child's dental health.

Thank you very much for taking the time to complete this questionnaire.

Instructions for completing the questionnaire:

For most questions we would like you to put an 'X' in the relevant box. Please use black ink and keep the cross inside the box:

Example: **Who typically carries out the toothbrushing?** tick **one** box only

the child on their own

the child, observed by an adult

adult brushes the child's teeth

If you need to correct an item draw a single line through it and write in the correct answer as shown:

Example: **Who typically carries out the toothbrushing?** tick **one** box only

the child on their own

the child, observed by an adult


adult brushes the child's teeth

For some questions you will need to write your answer. Please use **BLOCK CAPITALS**, e.g.

Example:
Occupation **TEACHER**

Or numbers as appropriate, e.g.

Example:
How many minutes did the appointment take including travel time? **048**



1.

Part A: Your child and their normal dental routine

1 Please confirm the following information about your child:

your child's initials:

your child's gender: Male Female

your child's date of birth (dd/mm/yyyy):

2 How often does your child brush their teeth? tick **one** box only

less than once a day

once a day

twice a day

more than twice a day

never skip to **→ Q7**

3 Who typically carries out the toothbrushing? tick **one** box only

the child on their own

the child, observed by an adult

adult brushes the child's teeth

4 What type of toothpaste does your child usually use? tick **one** box only

normal family toothpaste

children's toothpaste

other (fill in below)

5 How much toothpaste does your child usually use when brushing? tick **one** box only

a smear on the brush

a pea sized amount

cover the brush bristles

6 At what age did you start brushing your child's teeth? write age in the box below

Years Months

7 Is your child currently using any of the following? tick any that apply

	Yes	No	Brand
Mouthwash	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Fluoride drops	<input type="checkbox"/>	<input type="checkbox"/>	
Fluoride tablets	<input type="checkbox"/>	<input type="checkbox"/>	

8 Has your child ever had fluoride varnish or gel applied by their dentist? tick **one** box only

Yes No

Don't know

9 Does your child attend a dentist for check-ups? tick **one** box only

Yes

No skip to **→ Q11**

2.

10 How often does your child normally see the dentist? Tick **one** box only - fill in months if applicable

every months
only when in pain

11 Has your child lived in South Wales all their life?

Yes No

12 How often does your child eat or drink the following?

	Never	<1 per week	2-3 times per week	4-6 times per week	1 per day	2-3 times per day
Milk	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Water	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fizzy drinks	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Squash	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fruit juice	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Diet / light drinks / low sugar squash	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Sweets / Confectionery	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Chocolate	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Crisps	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fruit e.g. apples and bananas	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Cakes and biscuits	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
High fibre / low sugar breakfast cereals, like porridge, Weetabix and Shredded Wheat	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other breakfast cereals like Crunchy Nut Cornflakes, Frosties, Coco Pops	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Part B: Time taken up looking after your child's dental health

13 Not counting the mobile dental clinic at your child's school, has your child attended any other dental appointments in the last 12 months? Tick **one** box only

Yes How many times

No skip to **→Q15**

3.

14 For each appointment in the last 12 months, please list the following

Tick **one** box in each column

What was the reason for your appointment?	Appointment 1	Appointment 2	Appointment 3	Appointment 4
Toothache	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Check-up	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Filling	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Extraction	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other (write below)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Where did you receive the treatment?	Appointment 1	Appointment 2	Appointment 3	Appointment 4
Family Dentist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Emergency Dentist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Hospital Dentist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Doctor	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other (write below)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

How many minutes did the appointment take including travel time?	Appointment 1	Appointment 2	Appointment 3	Appointment 4
	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

How many miles did you have to travel to the appointment?	Appointment 1	Appointment 2	Appointment 3	Appointment 4
	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

How did you travel to the appointment?	Appointment 1	Appointment 2	Appointment 3	Appointment 4
Car	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
By foot	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Taxi	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Bus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Train	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other (write below)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Did you have to take time off paid work?	Appointment 1	Appointment 2	Appointment 3	Appointment 4
Yes	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
No	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

- 15** Has your child been prescribed (e.g. by a dentist/GP) any medicines for tooth related problems? Tick **one** box only

Yes

No skip to **→Q17**

- 16** What was the medicine that was prescribed? Tick as many as apply

	Yes	No	How many times
Pain relief medication (calpol, junior ibuprofen)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/>
Antibiotics	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/>
Other (write below)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/>

- 17** Over the past 12 months have you self-treated your child (without going to the dentist/GP) for a dental problem?

Tick **one** box only

Yes

No

If **Yes**, specify the treatment given

Painkillers

Other (write below)

- 18** Approximately how many days do you think your child has lost from school over the last 12 months due to dental problems and/or dental visits?
write number of days in box

Days

- 19** Did you or another carer need to take time off paid work or find yourself unable to undertake normal daily activities because of your child's dental problems or visits?
Tick **one** box only

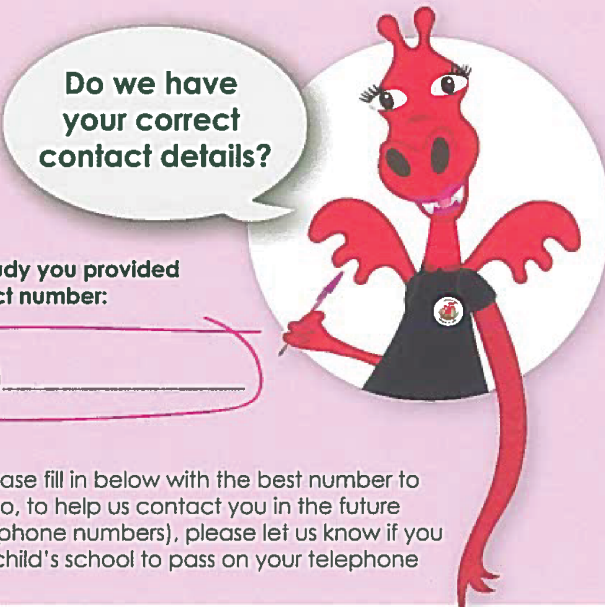
Yes

No

- 20** Could you describe the, present occupation of the child's main parent(s) or carer(s)?
write in box below

→PTO

5.



Do we have your correct contact details?

At the start of the study you provided the following contact number:

Tel. (_____) _____

If this is not right, please fill in below with the best number to contact you on. Also, to help us contact you in the future (e.g. if you change phone numbers), please let us know if you are happy for your child's school to pass on your telephone number.

The best number to reach me on is: Tel. (_____) _____

I give my permission for my child's school to pass on my current telephone number to the study team if they are unable to contact me in future please tick

Parent Name: _____

Signature: _____

When completed, please return to the SEWTU office using the pre-paid envelope provided.

Thank you very much!




SEWTU USE ONLY


Date received by SEWTU: / / Received by (initials):


Date entered onto database: / / Entered by (initials):

SoV QDH dental health postal questionnaire.doc (v2.1 - 07Aug2013)

Appendix 14 Child Health Utility Index 9D questionnaire


 29612





For office use only:

School ID:
Participant ID:
Baseline
12 mo
24 mo
36 mo

Seal or Varnish Study - 'Child Health Utility' Questionnaire

Dear Parent,

Please ask your child to answer the following questions. You may help your child if needed, but the answers should be from the child's point of view.

Before asking your child the questions, please confirm the following information:

1. Child's initials: 2. Child's Date of Birth (dd/mm/yyyy): / / 3. Gender: Male
 Female

These questions ask about how you are today. For each question, read all the choices and decide which one is most like you today. Then put a tick in the circle box next to it like this: ✓
 Only tick one circle for each question.

Example

Today I feel **quite upset** so I will tick this circle:

Upset

- I don't feel upset today
- I feel a little bit upset today
- I feel a bit upset today
- I feel quite upset today
- I feel very upset today

Now think about and answer the rest of the questions below (and on page 2)

A. Worried

- I don't feel worried today
- I feel a little bit worried today
- I feel a bit worried today
- I feel quite worried today
- I feel very worried today

B. Sad

- I don't feel sad today
- I feel a little bit sad today
- I feel a bit sad today
- I feel quite sad today
- I feel very sad today

C. Pain

- I don't have any pain today
- I have a little bit of pain today
- I have a bit of pain today
- I have quite a lot of pain today
- I have a lot of pain today

D. Tired

- I don't feel tired today
- I feel a little bit tired today
- I feel a bit tired today
- I feel quite tired today
- I feel very tired today



29612

E. Annoyed

- I don't feel annoyed today
- I feel a little bit annoyed today
- I feel a bit annoyed today
- I feel quite annoyed today
- I feel very annoyed today

F. School work/Homework (such as reading, writing, doing lessons)

- I have no problems with my schoolwork/homework today
- I have a few problems with my schoolwork/homework today
- I have some problems with my schoolwork/homework today
- I have many problems with my schoolwork/homework today
- I can't do my schoolwork/homework today

G. Sleep

- Last night I had no problems sleeping
- Last night I had a few problems sleeping
- Last night I had some problems sleeping
- Last night I had many problems sleeping
- Last night I couldn't sleep at all

H. Daily routine (things like eating, having a bath/shower, getting dressed)

- I have no problems with my daily routine today
- I have a few problems with my daily routine today
- I have some problems with my daily routine today
- I have many problems with my daily routine today
- I can't do my daily routine today

I. Able to join in activities (like playing out with your friends, doing sports, joining in things)

- I can join in with any activities today
- I can join in with most activities today
- I can join in with some activities today
- I can join in with a few activities today
- I can join in with no activities today

When completed please return to the SEWTU Office using the pre-paid envelope provided.

Thank you
very much!



FOR OFFICE USE ONLY:

Date received by SEWTU: / /

Received by (initials):

Date entered onto database: / /

Entered by (initials):

Appendix 15 Serious adverse event form

Seal or Varnish
Serious Adverse Reaction (SAE) Report Form
 EudraCT number: 2010-023476-23 Sponsor Number: SPON766-09
Submit completed SAE Report Form within 24hrs of becoming aware of the SAE.
 Secure fax number: 029 2068 7612 FAO: Seal or Varnish Trial Manager



Report Type: Initial Follow-up Final **Report Date:** []/[]/[]

Details of participant affected by SAE

School ID [] [] [] **Participant ID** [] [] [] **Initials** [] [] [] **Date of Birth** []/[]/[] **Gender** M F

Details of SAE (continue on separate sheet if necessary)

Onset Date: []/[]/[] **End date:** []/[]/[] **Duration:** []

Occurrence of Event reported by: Member of Dental Team Parent

Date trial site aware of event: []/[]/[]

SAE outcome: Resolved Ongoing Ongoing with sequelae Died Unknown

Main event or reaction: Please state a single event or reaction

Full description of event or reaction, including location event took place, body site, reported signs and symptoms and diagnosis, treatments received, actions taken. (Please include results of relevant test if appropriate):

If event results in death, please confirm cause of death (or state N/A):

The event is SERIOUS because it (tick as many as apply):

- Resulted in death
- Is or was life-threatening
- Resulted in hospitalisation
- Prolonged an existing hospitalisation
- Resulted in persistent or significant disability on incapacity
- Resulted in a congenital anomaly or birth defect
- Other event which required intervention to prevent any of the above outcomes

If other, please specify

Details of Investigational Medicinal Product(s) / Intervention

Name of IMP(s) / Intervention	Total dose administered	Date dose first administered dd/mm/yyyy	Date of last dose or state ongoing	Is the SAE related to the IMP / Intervention? 1= Definitely* 2=Probably* 3= Possibly* 4= Unlikely 5=Not assessable	Action taken (e.g. none, treatment reduced, treatment stopped)

NAME: _____ **Signature:** _____ **Date:** []/[]/[]

Seal or Varnish
SAE report form v1.0 18.03.2014

For office use only
SAE number:

**Seal or Varnish
Serious Adverse Reaction (SAE) Report Form**
 EudraCT number: 2010-023476-23 Sponsor Number: SPON766-09
Submit completed SAE Report Form within 24hrs of becoming aware of the SAE.
 Secure fax number: 029 2068 7612 FAO: Seal or Varnish Trial Manager



Details of other treatment (including concomitant medication, surgery, radiotherapy, etc) Do not give details of therapy given to manage SAE.					
Treatment name	Drug Dose (including units)	Route of administration (e.g oral, intravenous,etc)	Date first administered dd/mm/yyyy	Date & Time (24h clock) last administered or state ongoing	Action taken (e.g. none, treatment reduced, treatment stopped)

Further information relevant to assessment (e.g medical history, family history, test results):

I CONFIRM THAT THE CONTENTS OF THIS FORM ARE ACCURATE AND COMPLETE						
Name of person making report:						
Telephone number:						
Fax Number:						
PRINCIPAL INVESTIGATOR'S SIGNATURE			DATE:	DD	MM	YYYY

Submit a copy of the completed form to SEWTV Seal or Varnish Trial Manager within 24hrs of becoming aware of the SAE by secure fax to 029 2068 7612

Where complete information is not available at the time of the initial report, the principal investigator should submit a follow-up report as soon as possible.

FILE ORIGINAL IN TRIAL SITE FILE

Seal or Varnish
SAE report form v1.0 18.03.2014

For office use only SAE number:
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Seal or Varnish

Serious Adverse Reaction (SAE) Report Form

EudraCT number: 2010-023476-23 Sponsor Number: SPON766-09

Submit completed SAE Report Form within 24hrs of becoming aware of the SAE.

Secure fax number: 029 2068 7612 FAO: Seal or Varnish Trial Manager




For office use only:					
CHIEF INVESTIGATOR / CLINICAL REVIEWER DELEGATE ASSESSMENT					
	Was the SAE drug related? 1= Definitely* 2= Probably* 3= Possibly* 4= Unlikely 5= Not assessable			Was the SAE listed as expected on the approved Reference Safety Information? Please circle	
Delton / Duraphat				Yes	No
COMMENTS:					
NAME:					
SIGNATURE:				DATE:	DD MM YYYY
SEWTU ADMINISTRATION					
Date SAE form received at SEWTU: (day zero)	DD	MM	YYYY	Received by: (Print name)	
Date sent to clinical reviewer	DD	MM	YYYY	Clinical Reviewer: (Print name)	
Reference Safety Information date:	DD	MM	YYYY		
EVENT CATEGORISATION: (Please tick)	<input type="checkbox"/> SAE <input type="checkbox"/> SAR <input type="checkbox"/> 15 day SUSAR <input type="checkbox"/> 7 day SUSAR				
For SUSARs only:					
Date reported to MHRA:	DD	MM	YYYY		
Date reported to Ethics:	DD	MM	YYYY		
Date reported to Sponsor:	DD	MM	YYYY		
Date reported to	DD	MM	YYYY		
SEWTU STAFF SIGNATURE:				DATE:	DD MM YYYY

Seal or Varnish
SAE report form v1.0 18.03.2014

For office use only
SAE number:


Appendix 16 Dental hygienist observation scale



28727

QOH: SoV Observation Form (HYGENIST)

This form should be completed by the Dental HYGENIST during each treatment visit



SEAL OR VARNISH

1. School ID:

2. Participant ID:

3. Initials:

4. Date of Birth (dd/mm/yyyy): / /

5. Gender: Male Female

6. Visit: Baseline 6 month 12 month 18 month 24 month 30 month

7. Adverse outcomes observed:
Tick one box in each row

	Yes	No
Vomiting	<input type="checkbox"/>	<input type="checkbox"/>
Gagging	<input type="checkbox"/>	<input type="checkbox"/>
Crying	<input type="checkbox"/>	<input type="checkbox"/>
Excessive arm movements	<input type="checkbox"/>	<input type="checkbox"/>
Excessive leg movements	<input type="checkbox"/>	<input type="checkbox"/>
Other signs of distress (specify below)	<input type="checkbox"/>	<input type="checkbox"/>

8. Date form completed (dd/mm/yyyy): / /

9. Completed by: (please sign)

SEWTU USE ONLY
SoV QOH obs scale hygenist (v1.0 29Jul2011)

Date received by SEWTU: / /

Date entered onto database: / /

Received by (Initials):

Entered by (Initials):

Appendix 17 Children interview schedule

PRELIM

- What is your name and year in school?
- [Introduction of researcher]
- [Explanation of study and confidentiality, and why asking questions]

IMPLEMENTATION

- What did you think of visiting the dental van on school grounds during the school day?
- How did leaving your classroom and going to the dental van affect your normal school day?

TRIAL IMPLEMENTATION

- What did you think about coming for treatment? Have you been in the dental van before you got this treatment? Have any of your brothers or sisters been in the dental van? Do you have a local dentist?
- What do your friends think of you getting this dental treatment? What do people in your class think? What does your family think of you getting this dental treatment?
- How did you find filling in the forms in the van after your treatment? [prompt for whether they are easy/difficult]

TREATMENT ACCEPTABILITY

- What did you think of the dental treatment you got? What did you like or not like? [Prompt for taste: length of treatment, dental equipment, things explained by staff].
- Were your friends with you when you had the treatment? Did that make you feel any differently about it?
- Have you been to a dentist before? How was the dental van visit different from that?
- How would you feel about going back to the dental van and having the treatment again?

RECEPTION

- Do you think your teeth are any different since you had the treatment?
- Did your teeth change colour after the treatment? How did that affect you?
- Since you had this treatment, have you changed how you look after your teeth? [Prompt for changes in eating sweets and soda, changes in how often brush teeth, visits to dentist]

Appendix 18 Participating parents interview schedule

PRELIM

- [Introduction of researcher and purpose of study]
- [Explanation of confidentiality]
- What is your name, the name of your child and their year in school?

TRIAL IMPLEMENTATION

- What were your reasons for deciding to participate in the study? Were you influenced by family and friends in your decision? [prompt also for existing use of dental services and any difference this made]
- What did you think of the information sheet and forms you received about the study? [prompt for understanding of study purpose, what intervention involves and consent]
- Did you have any problems or concerns when you joined the study? [prompt for ease of joining, perceptions of treatment, contact taking place via school, concerns about losing place at local dentist, being comfortable with trial element, being comfortable with randomisation]
- Overall how did you find the experience of joining the study?

IMPLEMENTATION

- What do you think about your child receiving treatment in a school setting? [prompt for being removed from classroom for treatment, receiving treatment in a mobile dental clinic]
- How do you think your child felt about receiving treatment in the school setting? [prompt for being removed from classroom for treatment, receiving treatment in a mobile dental clinic]

TREATMENT ACCEPTABILITY

- How do you think your child felt about receiving the treatment? [prompt for taste, discomfort, time taken]
- How do you think receiving treatment in the mobile dental clinic compares to your child's normal dental care [prompt for whether have usual dentist and whether family is familiar with mobile dental clinics]

RECEPTION

- Do you think your child's teeth have changed in any way since they received the treatment? If so, how? [prompt for whether they feel they are more or less likely to get caries]
- Did your child experience any discolouration of their teeth and if so how did it affect them?
- Have you changed anything about how you take care of your child's teeth since joining the study? [prompt for diet, tooth brushing and visiting local dentist, receiving fluoride or other treatment]

Appendix 19 School/head teachers interview schedule

IMPLEMENTATION

- What do you remember about being initially approached for this study?
- How did you find the recruitment process for this study? [prompt for clarity of information, understanding of intervention and trial aspect, dealing with parents, communicating with dental team]
- How did you find working with dental team for the study, in comparison to the Smile programme, once the intervention was underway?
- Were there any particular barriers or problems in having the study at your site, compared to the usual Smile programme?
- What impact did having the dental van on school grounds make?
- Did the study have an impact on the school day for staff or children, such as creating extra paperwork or removing children from lessons?
- Did being part of the study change your communications with parents once the trial was underway?

TRIAL IMPLEMENTATION

- What do you think are the reasons for some parents not wanting to participate in the trial?
- Are you aware of any parents who withdrew from the trial, and if so what their reasons were?
- Were there particular groups or types of parents who you think were underrepresented in the trial?

RECEPTION

- How do you think children who participated in the study felt about their teeth after treatment? (if had any comments from them)

Appendix 20 Community dental staff interview schedule

IMPLEMENTATION

- How did you find delivering the treatment in this trial?
- How did you find working with schools and school staff in delivering an intervention in a trial setting?
- How did you find delivering the treatment in a van in school grounds?
- Were there any difficulties with identifying children and removing them from the classroom, compared to the “Designed to Smile” programme?
- Were there any differences in delivering the PFS compared to FV?
- Did being part of the trial affect how you delivered the PFS and FV treatment compared to the normal “Designed to Smile” programme? [prompt for how children are removed from classroom, number of staff in team, paperwork, getting children to complete scales]
- Did you experience any problems/barriers in delivering the treatment itself or additional work (such as forms) for the trial?

ACCEPTABILITY OF TREATMENT

- What responses have you seen to both PFS and FV treatments?
- Based on delivering the treatments, do you think children find PFS or FV more acceptable?

Appendix 21 Non-participating parents interview schedule

PRELIM

- What is your name, the name of your child and their year in school?
- [Introduction of researcher and purpose of study]
- [Explanation of confidentiality]

TRIAL IMPLEMENTATION

- What were your reasons for deciding not to participate in the study? Were you influenced by family and friends in your decision?
- Did you have any particular problems or concerns about joining the study? [prompt for ease of joining, perception of treatment, contact taking place via school, concerns about losing place at local dentist, being comfortable with trial element]
- What did you think of the information sheet and forms you received about the study? [prompt for understanding of study purpose, what intervention involves and consent]
- Overall how did you find the experience of being contacted about the study?

Appendix 22 Schools questionnaire

1. Thinking about how you found the initial approach about Seal or Varnish taking place in your school, what was your experience? (Please tick all that apply)

- It was time consuming
- It was straightforward
- The material was easy to understand
- Interesting to be part of a study
- Concerned about parent reaction
- Concerned about teacher reaction
- Concerned about extra disruption to classes
- Thought it would be very similar to current arrangement with mobile dental clinics visiting school
- Thought it would be a lot more work or disruption compared to current arrangement with mobile dental clinics visiting school
- Thought it would enhance image or reputation of school
- Concerned it would have an adverse impact on image or reputation of school
- Other:

2. What was your actual experience in relation to any concerns that you had?

3. Were there any particular problems or barriers to hosting Seal or Varnish that affected you or other staff who were involved in helping coordinate Seal or Varnish activity in your school?

- Explaining the study to parents
- Explaining the study to teachers
- Explaining the study to children
- Communicating with members of dental or study teams about the trial
- Finding time to respond to requests for data [interviews, questionnaires – including this one]

Other: [Click here to enter text.](#)

4. Did the school provide any assistance with recruiting parents e.g. phoning up particular parents to remind them about the study? If so, what type of staff member did this e.g. (administrator, teacher)?

[Click here to enter text.](#)

5. Can you describe how you found coordination with the dental teams both before, during and after visits by the mobile dental clinics?

a) Communicating before and after visit of mobile dental clinic to the school:

- Very easy/no problems
- Somewhat difficult/a few problems
- Very difficult/lots of problems

Please explain: [Click here to enter text.](#)

b) Organising child visits to mobile dental clinics around other school activities:

- Very easy/no problems
- Somewhat difficult/a few problems
- Very difficult/lots of problems

Please explain: [Click here to enter text.](#)

6. What impact did participating in Seal or Varnish have on the school day, including removing children from classrooms for treatment?

- Major impact Minor impact No difference

Please explain:

[Click here to enter text.](#)

7. On average, how much time did each child spend away from their class/usual school activities to attend each clinic visit?

Approximately minutes per child

8. On average, how much time was given by the teacher (time away/disruption from their normal teaching duties) to support each clinic visit (e.g. to enable the child to leave/return to the classroom)?

You may answer either by indicating the teaching time per child or the overall teacher time taken away from usual classroom activities for each mobile dental clinic visit.

Approximately minutes per child **OR** minutes per mobile dental clinic visit.

Please indicate the grade/spine point of the classroom teacher involved.

Grade/spine point

9. On average, how much classroom assistant/other teaching staff time was given to support each clinic visit?

You may answer either by indicating the teaching time per child or the overall teacher time taken away from usual classroom activities for each clinic visit.

Approximately minutes per child **OR** minutes per clinic visit.

Please indicate the grade/spine point of the teaching staff/classroom assistant support involved.

Grade/spine point

10. Did Seal or Varnish create extra work (including paperwork) for the school and if so how significant was this?

No difference A little more paperwork A lot more paperwork

11. Please list any school administrative/clerical support time for administrative tasks undertaken to support the programme. This should include:

a) support to set up/administer the study in your school (e.g. sending out study information, responding to parental queries, speaking to the research team)

Administrative task	Grade/spine point of staff	Approximate time per task (minutes)
<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>

b) support for each clinic visit (e.g. contacting parents if child is upset/unwell after the clinic visit)

Administrative task	Grade/spine point of staff	Approximate time per task (minutes)

12. Please list any other school resources or consumables (e.g. photocopying, telephone) used to support the programme.

Resource/consumable used	Approx number/minutes used

13. Was Seal or Varnish integrated with or used to support any existing policies or programmes (such as ‘Healthy Schools’) already operating in your school?

Yes No Don't know

Please explain:

Click here to enter text.

14. Did Seal or Varnish affect your communications with parents (e.g. did you receive phone calls about it)?

Yes No Don't know

Please
explain:

Click here to enter text.

15. Do you think having Seal or Varnish in your school changed how the participating children felt about their teeth after treatment (if they made any comments about it in school)?

Yes No Don't know

Please explain: Click here to enter text.

16. Do you think the participating children, and their parents, changed how they look after the child's teeth as a result of being part of Seal or Varnish (if they made any comments about it in school)?

Yes No Don't know

Please explain: Click here to enter text.

17. Do you have an idea of which parents did not participate in Seal or Varnish: if there were particular groups who did not participate?

- Children in families already engaged with health and dental services were *more* likely to participate
- Children in families already engaged with health and dental services were *less* likely to participate
- Children whose parents who speak little English were *more* likely to participate

- Children whose parents who speak little English were *less* likely to participate
- Children who receive free school meals were *more* likely to participate
- Children who receive free schools meals were *less* likely to participate

Other parents who were less likely to participate: [Click here to enter text.](#)

Reasons for non participation: [Click here to enter text.](#)

18. So far, have there been any types of parents who were more likely to withdraw their child from Seal or Varnish?

- Children whose parents who speak little English were *more* likely to withdraw
- Children whose parents who speak little English were *less* likely to withdraw
- Children who receive free school meals were *more* likely to withdraw
- Children who receive free schools meals were *less* likely to withdraw
- We haven't had any parents withdraw their children from the study yet
- Don't know

Please comment on any reasons for withdrawal from Seal or Varnish that you are aware of:

Click here to enter text.

Thank you. Please return this questionnaire to:

ScobleC@cardiff.ac.uk, or by post in the envelope provided.

Appendix 23 Non-participating parents questionnaire

We are interested in reasons why some parents may not wish their child to take part in the Seal or Varnish dental study. We would be grateful if you could complete this questionnaire – answers are confidential and will have no impact on any future dental treatment of you or your child. We will use this information to help us design future dental studies and services. Please only complete this if you did NOT give consent for your child to receive treatment as part of the study. Thank you.

I did not want my child to take part in the dental study because (tick as many as apply):

- I did not understand what the study would involve
- I wanted my child to continue their normal treatment from the mobile dental clinic and didn't want them to receive anything different
- I wanted my child to continue with their current/normal dental treatment at a local dental surgery
- I was afraid my child might lose their place at the local NHS dentist if they went somewhere else for treatment
- I wasn't confident that the treatment would be good for my child
- My child did not want the treatment and I did not want to make them have it
- I was worried about what a dental examination might find in my child's teeth
- I do not like the school being involved in or knowing too much about my child's health care
- I do not like taking part in research
- I did not like being unable to choose which treatment my child received in the study
- I did not want to have to fill out questionnaires for the study
- I did not want to be interviewed for the study
- Other (please state): _____

Please tell us a bit about your normal dental habits (please tick all that apply):

- My child currently has a regular dentist at a local surgery
- My child is currently receives treatment from the 'Designed to Smile' programme (in the mobile dental clinics which visit the school)
- My child has never visited the dentist before

Appendix 24 Participant withdrawal form (version 2.1)



Participant Withdrawal Form

This form should be completed when a participant is withdrawn (either by the Investigator or at the parent's request)

1. School ID: 2. Participant ID:

3. Initials: 4. Date of Birth:

5. Gender: Male
 Female

WITHDRAWAL DETAILS:

6. Date of Withdrawal:

7. Nature of Withdrawal:

- (a) Child moved to non-participating school
- (b) Withdrawal of parental consent
- (c) Withdrawn for clinical reasons

8. Extent of Withdrawal (*Tick all that apply following discussion with parent*): -

- (a) No further treatment to be given
- (b) No further clinical examinations to be performed
- (c) Consent for child to receive remaining annual examinations
- (d) Consent for child to be examined at 36 month timepoint only
- (e) Consent for use of all existing data collected in analysis
- (f) Consent for QDH & QCH-9UD Questionnaires to be sent for remainder of study
- (g) NOT APPLICABLE – child moved to non-participating school

9. Reason for Withdrawal (*please indicate if withdrawing parent does not provide a reason*):

Completed by: (Please Sign) Date completed:

For SEWTU use ONLY:


Date received:

Date entered on database:

Entered by:

Seal or Varnish Withdrawal Form v2.1 – 17 June 2014


Appendix 25 Dental nurse observation scale (version 1.0)



42428

QON: SoV Observation Form (NURSE)

This form should be completed by the Dental NURSE during each treatment visit



SEAL OR VARNISH

1. School ID:

2. Participant ID: 3. Initials: 4. Date of Birth (dd/mm/yyyy): / / 5. Gender: Male Female

6. Visit: Baseline 6 month 12 month 18 month 24 month 30 month

7. Adverse outcomes observed:
Tick one box in each row

	Yes	No
Vomiting	<input type="checkbox"/>	<input type="checkbox"/>
Gagging	<input type="checkbox"/>	<input type="checkbox"/>
Crying	<input type="checkbox"/>	<input type="checkbox"/>
Excessive arm movements	<input type="checkbox"/>	<input type="checkbox"/>
Excessive leg movements	<input type="checkbox"/>	<input type="checkbox"/>
Other signs of distress (specify below)	<input type="checkbox"/>	<input type="checkbox"/>

8. Time taken to perform the application:
Please list the number of minutes and seconds from when the child was seated for the procedure until the child was able to leave the dental chair.

Minutes

Seconds


9. Date form completed (dd/mm/yyyy): / / 10. Completed by: (please sign)

SEWTU USE ONLY
SoV QON obs scale nurse (v1.0 29Jul2011)


Date received by SEWTU: / / Received by (initials):

Date entered onto database: / / Entered by (initials):


Appendix 26 F00 study eligibility case report form (version 2.3)



Synllun Gwên
Designed to smile



SEAL OR VARNISH



NHTA
NHR Health Technology Assessment programme funded by NIHR

F00: SoV Study Eligibility Form

This form should be completed by the Dental Nurse at the screening examination

1. School ID

Section 1: Participants Details

2. Participant ID

3. Initials

4. Date of Birth

5. Gender Male Female

6. Date of Eligibility Assessment

7. Does the child meet the inclusion criteria? Yes No

a.	Is the child in Year 2, (aged 6-7 years), attending a school participating in the current Cardiff & Vale UHB Designed to Smile Programme?	<input type="checkbox"/>	<input type="checkbox"/>
b.	Has the person with parental responsibility provided written informed consent for the child	<input type="checkbox"/>	<input type="checkbox"/>

8. Does the child meet any of the exclusion criteria?

a.	Does the child have a medical history that precludes inclusion (i.e. those with a history of hospitalisation for asthma, or severe allergies, or allergy to Elastoplast) ?	<input type="checkbox"/>	<input type="checkbox"/>
b.	Does the child have any known sensitivity to colophony (kolophonium), or any of the product ingredients (e.g. methylacrylate in PFS)?	<input type="checkbox"/>	<input type="checkbox"/>
c.	Is the child currently participating in another clinical trial involving an investigational medicinal product ?	<input type="checkbox"/>	<input type="checkbox"/>
d.	Does the child have ulcerative gingivitis or stomatitis ?	<input type="checkbox"/>	<input type="checkbox"/>
e.	Does the child have any facial or oral infections e.g. cold sores ?	<input type="checkbox"/>	<input type="checkbox"/>
f.	Does the child have any abnormality of the lips, face or soft tissues of the mouth that would cause discomfort in the provision of PFS/FV ?	<input type="checkbox"/>	<input type="checkbox"/>
g.	Does the child show obvious signs of systemic illness (e.g. colds, 'flu, chicken pox etc) ?	<input type="checkbox"/>	<input type="checkbox"/>

The child must meet ALL of the inclusion criteria and NONE of the exclusion criteria to be recruited into the study

9. Is the child eligible for participation? Yes -> The first permanent molar eligibility (Page 2) should now be completed

No -> The child may still participate in the fissure sealant programme if eligible and parent has given consent

PLEASE COMPLETE ITEMS 19, 20 AND 21 ON PAGE 4

F00 SoV Eligibility Form Version 2.3

05/09/2011



First Permanent Molar Eligibility

<p>UPPER RIGHT</p> <p>10. Suitable for sealant or varnish Yes No <input type="checkbox"/> <input type="checkbox"/></p> <p>If not suitable state reason (tick one)</p> <p>a. Tooth unerupted <input type="checkbox"/></p> <p>b. Exclude tooth due to caries into dentine <input type="checkbox"/></p> <p>c. Exclude tooth due to extraction <input type="checkbox"/></p> <p>d. Exclude tooth due to filling <input type="checkbox"/></p> <p>e. Exclude tooth due to sealant <input type="checkbox"/></p> <p>f. Exclude tooth due to hypoplasia <input type="checkbox"/></p>	<p>UPPER LEFT</p> <p>11. Suitable for sealant or varnish Yes No <input type="checkbox"/> <input type="checkbox"/></p> <p>If not suitable state reason (tick one)</p> <p>a. Tooth unerupted <input type="checkbox"/></p> <p>b. Exclude tooth due to caries into dentine <input type="checkbox"/></p> <p>c. Exclude tooth due to extraction <input type="checkbox"/></p> <p>d. Exclude tooth due to filling <input type="checkbox"/></p> <p>e. Exclude tooth due to sealant <input type="checkbox"/></p> <p>f. Exclude tooth due to hypoplasia <input type="checkbox"/></p>
<p>LOWER RIGHT</p> <p>12. Suitable for sealant or varnish Yes No <input type="checkbox"/> <input type="checkbox"/></p> <p>If not suitable state reason (tick one)</p> <p>a. Tooth unerupted <input type="checkbox"/></p> <p>b. Exclude tooth due to caries into dentine <input type="checkbox"/></p> <p>c. Exclude tooth due to extraction <input type="checkbox"/></p> <p>d. Exclude tooth due to filling <input type="checkbox"/></p> <p>e. Exclude tooth due to sealant <input type="checkbox"/></p> <p>f. Exclude tooth due to hypoplasia <input type="checkbox"/></p>	<p>LOWER LEFT</p> <p>13. Suitable for sealant or varnish Yes No <input type="checkbox"/> <input type="checkbox"/></p> <p>If not suitable state reason (tick one)</p> <p>a. Tooth unerupted <input type="checkbox"/></p> <p>b. Exclude tooth due to caries into dentine <input type="checkbox"/></p> <p>c. Exclude tooth due to extraction <input type="checkbox"/></p> <p>d. Exclude tooth due to filling <input type="checkbox"/></p> <p>e. Exclude tooth due to sealant <input type="checkbox"/></p> <p>f. Exclude tooth due to hypoplasia <input type="checkbox"/></p>

14. Is the Child eligible for Seal or Varnish study (at least one tooth suitable)?

YES -> the ICDAS Caries Assessment chart (Page 3) should now be completed

NO -> (the child may still participate in the fissure sealant programme if eligible and parent has consented for this)

PLEASE COMPLETE ITEMS 19, 20 AND 21 ON PAGE 4



SEAL OR VARNISH



Cynllun Gwên
Designed to smile

UPPER RIGHT

6	E/5	D/4	C/3	B/2	A/1	
D	O	M	B	L	D	O
O	M	B	L	D	O	M
M	B	L	D	O	M	B
B	L	D	O	M	B	L
L	D	O	M	B	L	D

UPPER LEFT

A/1	B/2	C/3	D/4	E/5	6
D	O	M	B	L	D
O	M	B	L	D	O
M	B	L	D	O	M
B	L	D	O	M	B
L	D	O	M	B	L

LOWER RIGHT

6	E/5	D/4	C/3	B/2	A/1
D	O	M	B	L	D
O	M	B	L	D	O
M	B	L	D	O	M
B	L	D	O	M	B
L	D	O	M	B	L

LOWER LEFT

A/1	B/2	C/3	D/4	E/5	6
D	O	M	B	L	D
O	M	B	L	D	O
M	B	L	D	O	M
B	L	D	O	M	B
L	D	O	M	B	L

Corrections : _____
(Please number all corrections)

Now complete the Hypoplasia record (page 4) for the first permanent molars only

FOO SoV Eligibility Form Version 2.3

05/09/2011



First Permanent Molar Hypoplasia Record

UPPER RIGHT	UPPER LEFT
<p>15. Hypoplasia status (tick one)</p> <p>no hypoplasia <input type="checkbox"/></p> <p>demarked opacity <input type="checkbox"/></p> <p>post eruptive breakdown (excluded) <input type="checkbox"/></p> <p>tooth missing/unerupted <input type="checkbox"/></p>	<p>16. Hypoplasia status (tick one)</p> <p>no hypoplasia <input type="checkbox"/></p> <p>demarked opacity <input type="checkbox"/></p> <p>post eruptive breakdown (excluded) <input type="checkbox"/></p> <p>tooth missing/unerupted <input type="checkbox"/></p>
<p>17. Hypoplasia status (tick one)</p> <p>no hypoplasia <input type="checkbox"/></p> <p>demarked opacity <input type="checkbox"/></p> <p>post eruptive breakdown (excluded) <input type="checkbox"/></p> <p>tooth missing/unerupted <input type="checkbox"/></p>	<p>18. Hypoplasia status (tick one)</p> <p>no hypoplasia <input type="checkbox"/></p> <p>demarked opacity <input type="checkbox"/></p> <p>post eruptive breakdown (excluded) <input type="checkbox"/></p> <p>tooth missing/unerupted <input type="checkbox"/></p>
LOWER RIGHT	LOWER LEFT

19. Date form completed

20. Completed by (please sign)




21. Examining Dentist Initials

For SEWTU use only

Received: Received by: Entered into database:

Entered by: Randomisation Allocation: FS V

Appendix 27 C01 caries follow-up case report form (version 2.5)

C01: Caries Follow-up Assessment Form

This form should be completed by the Dental Nurse at the screening examination

1. School ID

Section 1: Participants Details

2. Participant ID

3. Initials

4. Date of Birth

5. Gender Male Female

6. Date of Treatment

7. Follow-up visit 12month 24month 36month

C01 Caries Follow-up Form, version 2.5 17/06/2014



Cynllun Gwên
designed to smile



SEAL OR VARNISH

UPPER RIGHT

6	E/5	D/4	C/3	B/2	A/1
D					
O					
M					
B					
L					
D					
O					
M					
B					
L					

UPPER LEFT

A/1	B/2	C/3	D/4	E/5	6
D					
O					
M					
B					
L					
D					
O					
M					
B					
L					

LOWER RIGHT

6	E/5	D/4	C/3	B/2	A/1
D					
O					
M					
B					
L					

LOWER LEFT

A/1	B/2	C/3	D/4	E/5	6
D					
O					
M					
B					
L					

Corrections : _____
(Please number all corrections)

Now complete the Hypoplasia Record for the first permanent molars only



First Permanent Molar Hypoplasia Record

UPPER RIGHT	UPPER LEFT
<p>8. Hypoplasia status (tick one)</p> <p>normal (tooth in trial) <input type="checkbox"/></p> <p>demarked opacity (tooth in trial) <input type="checkbox"/></p> <p>post eruptive breakdown (excluded) <input type="checkbox"/></p> <p>tooth missing <input type="checkbox"/></p>	<p>9. Hypoplasia status (tick one)</p> <p>normal (tooth in trial) <input type="checkbox"/></p> <p>demarked opacity (tooth in trial) <input type="checkbox"/></p> <p>post eruptive breakdown (excluded) <input type="checkbox"/></p> <p>tooth missing <input type="checkbox"/></p>
<p>10. Hypoplasia status (tick one)</p> <p>normal (tooth in trial) <input type="checkbox"/></p> <p>demarked opacity (tooth in trial) <input type="checkbox"/></p> <p>post eruptive breakdown (excluded) <input type="checkbox"/></p> <p>tooth missing <input type="checkbox"/></p>	<p>11. Hypoplasia status (tick one)</p> <p>normal (tooth in trial) <input type="checkbox"/></p> <p>demarked opacity (tooth in trial) <input type="checkbox"/></p> <p>post eruptive breakdown (excluded) <input type="checkbox"/></p> <p>tooth missing <input type="checkbox"/></p>
LOWER RIGHT	LOWER LEFT

12. Date form completed

13. Completed by
(please sign)


14. Examining Dentist Initials

For SEWTU use only


Received: Received by: Entered into database:

Entered by:


Appendix 28 C02 caries re-examination case report form (version 2.6)



Cynllun Gwên
Designed to smile



SEAL OR VARNISH



NIHR Health Technology Assessment Programme

C02: Caries Assessment Re-examination Form

This form should be completed by the Dental Nurse at the caries examination

1. School ID

Section 1: Participants Details

2. Participant ID

3. Initials

4. Date of Birth

5. Gender Male Female

6. Date of Assessment

7. Visit: Baseline 12month 24month 36 month

C02 Caries Re-examination Form Version 2.6 06/03/2013



Cynllun Gwên
designed to smile

SEAL OR VARNISH

UPPER RIGHT

6	E/5	D/4	C/3	B/2	A/1
D					
O					
M					
B					
L					

UPPER LEFT

A/1	B/2	C/3	D/4	E/5	6
D					
O					
M					
B					
L					

LOWER RIGHT

LOWER LEFT

Corrections : _____
(Please number all corrections)

Now complete the Hypoplasia Record for the first permanent molars only

C02 Caries Re-examination Form Version 2.6 06/03/2013

First Permanent Molar Hypoplasia Record

UPPER RIGHT	UPPER LEFT
8. Hypoplasia status (tick one) normal (tooth in trial) <input type="checkbox"/> demarked opacity (tooth in trial) <input type="checkbox"/> post eruptive breakdown (excluded) <input type="checkbox"/> tooth missing <input type="checkbox"/>	9. Hypoplasia status (tick one) normal (tooth in trial) <input type="checkbox"/> demarked opacity (tooth in trial) <input type="checkbox"/> post eruptive breakdown (excluded) <input type="checkbox"/> tooth missing <input type="checkbox"/>
10. Hypoplasia status (tick one) normal (tooth in trial) <input type="checkbox"/> demarked opacity (tooth in trial) <input type="checkbox"/> post eruptive breakdown (excluded) <input type="checkbox"/> tooth missing <input type="checkbox"/>	11. Hypoplasia status (tick one) normal (tooth in trial) <input type="checkbox"/> demarked opacity (tooth in trial) <input type="checkbox"/> post eruptive breakdown (excluded) <input type="checkbox"/> tooth missing <input type="checkbox"/>
LOWER RIGHT	LOWER LEFT

 12. Date form completed

 13. Completed by
 (please sign)

 14. Examining Dentist Initials

For SEWTU use only

 Received: Received by: Entered into database:

 Entered by:

C02 Caries Re-examination Form Version 2.6 06/03/2013

Appendix 29 F1S sealant baseline treatment record case report form (version 2.3)



F1S: SoV Sealant Baseline Treatment Record Form

This form should be completed by the Dental Hygienist at the baseline treatment visit

1. School ID

Section 1: Participants Details

2. Participant ID 3. Initials 4. Date of Birth

5. Gender Male Female

6. Date of Treatment

UPPER RIGHT		UPPER LEFT			
	Yes	No			
7. Is this tooth in the trial?	<input type="checkbox"/>	<input type="checkbox"/>	10. Is this tooth in the trial?	<input type="checkbox"/>	<input type="checkbox"/>
8. If yes, was a sealant placed ?	<input type="checkbox"/>	<input type="checkbox"/>	11. If yes, was a sealant placed ?	<input type="checkbox"/>	<input type="checkbox"/>
8a. Sealant bottle number			11a. Sealant bottle number		
8b. Sealant expiry date:			12b. Sealant expiry date:		
9. If no sealant placed state reason (tick one)			12. If no sealant placed state reason (tick one)		
Tooth unerupted / partially erupted	<input type="checkbox"/>		Tooth unerupted / partially erupted	<input type="checkbox"/>	
Tooth extracted	<input type="checkbox"/>		Tooth extracted	<input type="checkbox"/>	
Refused	<input type="checkbox"/>		Refused	<input type="checkbox"/>	
Other reason (please state)	<input type="checkbox"/>		Other reason (please state)	<input type="checkbox"/>	
9a.....			12a.....		
13. Is this tooth in the trial?	<input type="checkbox"/>	<input type="checkbox"/>	16. Is this tooth in the trial?	<input type="checkbox"/>	<input type="checkbox"/>
14. If yes, was a sealant placed ?	<input type="checkbox"/>	<input type="checkbox"/>	17. If yes, was a sealant placed ?	<input type="checkbox"/>	<input type="checkbox"/>
14a. Sealant bottle number			17a. Sealant bottle number		
14b. Sealant expiry date:			17b. Sealant expiry date:		
15. If no sealant placed state reason (tick one)			18. If no sealant placed state reason (tick one)		
Tooth unerupted / partially erupted	<input type="checkbox"/>		Tooth unerupted / partially erupted	<input type="checkbox"/>	
Tooth extracted	<input type="checkbox"/>		Tooth extracted	<input type="checkbox"/>	
Refused	<input type="checkbox"/>		Refused	<input type="checkbox"/>	
Other reason (please state)	<input type="checkbox"/>		Other reason (please state)	<input type="checkbox"/>	
15a.....			18a.....		
LOWER RIGHT			LOWER LEFT		

19. Date form completed 20. Completed by (please sign)

21. Treating Hygienist Initials

For SEWTU use only

Received: Received by: Entered into database:

Entered by:

F1S SoV Sealant Treatment Form, version 2.3 05/09/2011

Appendix 30 F1V varnish treatment record form (version 2.4)



F1V: SoV Varnish Treatment Record Form

This form should be completed by the Dental Hygienist at each treatment visit

1. School ID

Section 1: Participants Details

2. Participant ID 3. Initials 4. Date of Birth

5. Gender Male Female

6. Date of Treatment

7. Treatment visit: Baseline 6 month 12month 18month 24month 30month

UPPER RIGHT		UPPER LEFT	
8. Varnish applied?	Yes <input type="checkbox"/> No <input type="checkbox"/>	10. Varnish applied?	Yes <input type="checkbox"/> No <input type="checkbox"/>
8a. Varnish tube number:		10a. Varnish tube number	
8b. Varnish 'Use Before' date:		10b. Varnish 'Use Before' date:	
9. If varnish not applied state reason (tick one)		11. If varnish not applied state reason (tick one)	
Tooth unerupted <input type="checkbox"/>		Tooth unerupted <input type="checkbox"/>	
Tooth extracted <input type="checkbox"/>		Tooth extracted <input type="checkbox"/>	
Refused <input type="checkbox"/>		Refused <input type="checkbox"/>	
Other reason (please state) <input type="checkbox"/>		Other reason (please state) <input type="checkbox"/>	
9a.....		11a.....	
12. Varnish applied	Yes <input type="checkbox"/> No <input type="checkbox"/>	14. Varnish applied	Yes <input type="checkbox"/> No <input type="checkbox"/>
12a. Varnish tube number:		14a. Varnish tube number:	
12b. Varnish 'Use Before' date:		14b. Varnish 'Use Before' date:	
13. If varnish not applied state reason (tick one)		15. If varnish not applied state reason (tick one)	
Tooth unerupted <input type="checkbox"/>		Tooth unerupted <input type="checkbox"/>	
Tooth extracted <input type="checkbox"/>		Tooth extracted <input type="checkbox"/>	
Refused <input type="checkbox"/>		Refused <input type="checkbox"/>	
Other reason (please state) <input type="checkbox"/>		Other reason (please state) <input type="checkbox"/>	
13a.....		15a.....	
LOWER RIGHT		LOWER LEFT	

16. Date form completed

17. Completed by
(please sign)

18. Treating Hygienist Initials

For SEWTU use only

Received: Received by: Entered into database:

Entered by:

F1V SoV Varnish Treatment Form, v2.4 12.03.2012

Appendix 31 FTP treatment plan (version 1.2)



FTP: SoV Treatment Plan Form

This form should be completed by the Dental Examiner at Baseline for children eligible for the trial

1. School ID

Section 1: Participants Details

2. Participant ID 3. Initials 4. Date of Birth

5. Gender Male Female

6. Date of Examination

7. Visit Baseline 12month 24month

In accordance with the allocation to treatment group

8. **Either** apply fluoride varnish every six months to

6	6
6	6

(Delete teeth extracted at baseline)

Or apply fissure sealant/repair fissure sealant to

6	6
6	6

(Delete teeth extracted, carious or filled at baseline)

9. Date form completed

10. Completed by
(please sign)

Appendix 32 F2S sealant follow-up treatment record case report form (version 2.4)



F2S: SoV Sealant Follow-up Treatment Record Form

This form should be completed by the Dental Hygienist at each follow up treatment visit

1. School ID

Section 1: Participants Details

2. Participant ID 3. Initials 4. Date of Birth

5. Gender Male Female 6. Date of Treatment

7. Follow-up visit 6 month 12month 18month 24month 30month

UPPER RIGHT		UPPER LEFT	
	Yes No		Yes No
8. Is this tooth in the trial?	<input type="checkbox"/> <input type="checkbox"/>	11. Is this tooth in the trial?	<input type="checkbox"/> <input type="checkbox"/>
9. If yes what is the sealant status (tick one)		12. If yes what is the sealant status (tick one)	
Intact	<input type="checkbox"/>	Intact	<input type="checkbox"/>
Partially intact	<input type="checkbox"/>	Partially intact	<input type="checkbox"/>
Lost	<input type="checkbox"/>	Lost	<input type="checkbox"/>
Tooth unerupted / partially erupted	<input type="checkbox"/>	Tooth unerupted / partially erupted	<input type="checkbox"/>
Tooth extracted	<input type="checkbox"/>	Tooth extracted	<input type="checkbox"/>
Tooth previously unerupted/not sealed	<input type="checkbox"/>	Tooth previously unerupted/not sealed	<input type="checkbox"/>
10. Treatment record	Yes No	13. Treatment record	Yes No
Sealant placed/replaced/repared	<input type="checkbox"/> <input type="checkbox"/>	Sealant placed/replaced/repared	<input type="checkbox"/> <input type="checkbox"/>
10a. Sealant bottle number		13a. Sealant bottle number	
10b. Sealant expiry date		13b. Sealant expiry date	
If unable to complete required treatment state reason (e.g. refused)		If unable to complete required treatment state reason (e.g. refused)	
10c.....		13c.....	
LOWER RIGHT		LOWER LEFT	
	Yes No		Yes No
14. Is this tooth in the trial?	<input type="checkbox"/> <input type="checkbox"/>	17. Is this tooth in the trial?	<input type="checkbox"/> <input type="checkbox"/>
15. If yes what is the sealant status (tick one)		18. If yes what is the sealant status (tick one)	
Intact	<input type="checkbox"/>	Intact	<input type="checkbox"/>
Partially intact	<input type="checkbox"/>	Partially intact	<input type="checkbox"/>
Lost	<input type="checkbox"/>	Lost	<input type="checkbox"/>
Tooth unerupted / partially erupted	<input type="checkbox"/>	Tooth unerupted / partially erupted	<input type="checkbox"/>
Tooth extracted	<input type="checkbox"/>	Tooth extracted	<input type="checkbox"/>
Tooth previously unerupted/not sealed	<input type="checkbox"/>	Tooth previously unerupted/not sealed	<input type="checkbox"/>
16. Treatment record	Yes No	19. Treatment record	Yes No
Sealant placed/replaced/repared	<input type="checkbox"/> <input type="checkbox"/>	Sealant placed/replaced/repared	<input type="checkbox"/> <input type="checkbox"/>
16a. Sealant bottle number		19a. Sealant bottle number	
16b. Sealant expiry date		19b. Sealant expiry date	
If unable to complete required treatment state reason (e.g. refused)		If unable to complete required treatment state reason (e.g. refused)	
16c.....		19c.....	

20. Date form completed

21. Completed by
(please sign)

22. Treating hygienist Initials

For SEWTU use only

Received: Received by: Entered into database: Entered by:

F2S SoV Sealant Follow Up Treatment Form, v2.4 26/03/2012

Appendix 33 Letter to school (version 1.0)

<<To be produced on appropriate headed paper>>

Professor I.G. Chestnutt

Tel:

[DATE]

Dear Headteacher,

RE: Seal or Varnish a Clinical Trial – Pilot study

The National Health Service (Health Technology Assessment division) have commissioned a clinical trial to test two different methods of protecting children's teeth. The study is being carried out by the Cardiff University School of Dentistry. It will involve 920 children from Community First schools in South Wales aged between 6 and 7 years and the start of the study and follow them for thirty six months. The study will help to identify the best way of protecting the childrens' teeth from tooth decay.

The first stage of the study involves piloting the methods that will be used in the mainstage of the study. We hope that you will agree to let your school take part in the Pilot study to do this. We need to identify approximately 35 children aged between 6 and 7 years whose parents will consent to their child undergoing a dental examination.

Parent/guardians of children aged 6 to 7 will be sent a letter explaining the study and asking them to allow their child to take part in the study and undergo a short dental examination.

When the dentist visits the school they will require a room in which to carry out the examinations and some assistance in bringing the selected children to the room to be examined. The school will also need to keep a list of any children whose parents withdraw them from the study to give to the dentist when they visit the school.

I appreciate schools have many demands on their time but I hope you will feel able to help us. Participation in the study is voluntary. The dental visits are planned for the <<insert date>>. If you are able to take part please return the attached slip in the envelope provided so that I can arrange a date for the dentist to visit.

If you have any queries about the survey, please contact me, Professor Ivor Chestnutt on 029 2074 2447 / 6680.

Thank you.

Yours sincerely

Professor Ivor Chestnutt

School:

I am willing to allow my school to take part in the dental training exercise.

Signed: Head Teacher Date:

Appendix 34 Baseline examination follow-up letter (version 1.1)



Dear Parent/Guardian,

Your child's teeth were examined by a dentist today as part of the Seal or Varnish study.

The outcome of the examination was:

- Your child is suitable to be included in the study and will receive treatment in the next 2 to 4 weeks. Please do not give your child any fluoride-containing dental medication (tablets, gels etc) other than their normal fluoride toothpaste while your child is in the study.
- Your child is is not suitable to be included in the study, but his/her teeth may still be treated through the existing *Designed to Smile* programme
- Your child is is not suitable to be included in the study, and his/her back teeth are not yet ready to be treated through the *Designed to Smile* programme (because they have not yet come through into the mouth). The Mobile Dental Clinic will be back at your child's school next year when they will review their teeth again.

Are any other treatments required for my child's teeth?

- The dentist did not find anything during the examination that requires immediate attention. However if your child is registered with a dentist it is important to attend regularly.
- The dentist recommends that you make an appointment for your child to see a dentist for a more detailed examination **as further treatment may be necessary**. If your child is **not registered** with a family dentist or community clinic, please contact the *Designed to Smile* team on **02920 ******* who can help you find a dentist.

Seal or Varnish Baseline Exam follow-up letter Version 1.1 – 12Jul2011

Appendix 35 Clinical examination follow-up letter (version 2.0)



Dear Parent/Guardian,

Your child was seen by the Dental Team today as part of the Seal or Varnish study:

- Your child received fissure sealant. This will be checked again in 6 months and replaced if required.
- Your child received fluoride varnish and will have the same treatment applied in 6 months.

Information regarding the above treatments may be found in the 'Seal or Varnish' Information Booklet provided to you before the start of the study. If you would like to receive another copy of this booklet please call the study team on 02920 *****.

PLEASE LET US KNOW IF YOU CHANGE ADDRESS BY CALLING THE DENTAL TEAM ON 02920 *****

Seal or Varnish Initial Application follow-up letter Version 2.0 – 29May2012

Appendix 36 Consent follow-up letter (LR) (version 1.0)



Dear <<INSERT PARENT NAME>>,

Earlier in the school year you agreed for <<INSERT CHILD'S NAME>> to take part in the Seal or Varnish study, which is evaluating two different ways of protecting children's teeth from tooth decay. Unfortunately, the mobile dental unit was unable to see <<<<INSERT CHILD'S NAME>> at that time.

The mobile dental clinic will be returning to <<INSERT SCHOOL NAME>> during the next school year to check if <<INSERT CHILD'S NAME>> is suitable to take part in the study.

If you are still happy for <<INSERT CHILD'S NAME>> to take part in the study, we need to make sure they are still suitable to take part. Therefore we need you to let us know if there has been any significant change in <<INSERT CHILD'S NAME>>'s health in the last year by looking at the questions on page 2.

- If the answer is **YES** to **ANY** of the questions on the form, please complete the form and return it to the study team in the enclosed pre-paid envelope.
- If there has been **NO CHANGE** to <<INSERT CHILD'S NAME>>'s health in the last year you **DO NOT** need to return the form

If you have changed your mind and would **NOT** like <<INSERT CHILD'S NAME>> to take part in the study, or would like to discuss the study with a member of the dental team, please call the Community Dental Service on 02920*****.

Thank you!

The Seal or Varnish study team

Appendix 37 Consent follow-up letter (UE) (version 1.0)



Dear <<INSERT PARENT NAME>>,

Earlier in the school year you agreed for <<INSERT CHILD'S NAME>> to take part in the Seal or Varnish study, which is evaluating two different ways of protecting children's teeth from tooth decay. At the time <<INSERT CHILD'S NAME>>'s teeth were not quite ready to be treated because the back teeth had not come through enough, and therefore <<INSERT CHILD'S NAME>> was not able to participate in the study at that time.

The mobile dental clinic will be returning to <<INSERT SCHOOL NAME>> during the next school year to check if <<INSERT CHILD'S NAME>>'s teeth are now ready to be treated, and therefore able to take part in the study.

If you are still happy for <<INSERT CHILD'S NAME>> to take part in the study, we need to make sure they are still suitable to take part. Therefore we need you to let us know if there has been any significant change in the information you provided about <<INSERT CHILD'S NAME>>'s health last year. Please look at the questions on page 2.

- If the answer is **YES** to **ANY** of the questions on the form, please complete the form and return it to the study team in the enclosed pre-paid envelope.
- If there has been **NO CHANGE** to <<INSERT CHILD'S NAME>>'s health in the last year you **DO NOT** need to return the form

If you have changed your mind and would **NOT** like <<INSERT CHILD'S NAME>> to take part in the study, or would like to discuss the study with a member of the dental team, please call the Community Dental Service on 02920 *****.

Thank you!

The Seal or Varnish study team

Appendix 38 Interim visits follow-up letter (version 2.0)



Bwrdd Iechyd Prifysgol
Caerdydd a'r Fro
Cardiff and Vale
University Health Board



Dear Parent/Guardian,

Your child was seen by the Dental Team today as part of the Seal or Varnish Trial:

- The previous treatment (plastic sealant) your child received is still in place and did not need replacing. This will be checked again in 6 months and replaced if required.
- The previous treatment (plastic sealant) your child received had become dislodged/lost and was replaced with a new one. This will be checked again in 6 months and replaced if required.
- Your child received fluoride varnish and will have the same treatment applied in 6 months.

REMINDER:

Please do not give your child any fluoride-containing dental medication (tablets, gels etc) other than their normal fluoride toothpaste while your child is in the study.

PLEASE LET US KNOW IF YOU CHANGE ADDRESS BY CALLING THE DENTAL

TEAM ON 02920 *****

Seal or Varnish Interim Visit follow-up letter Version 2.0 – 29May2012

Appendix 39 Interim visits missed treatment follow-up letter (version 2.0)



Dear Parent/Guardian,

The Mobile Dental Clinic was at your child's school today as part of the Seal or Varnish study.

Your child was due to receive treatment today, but we were unable to carry out this treatment because they were:

- Uncooperative
- Feeling unwell
- Absent

We will be returning to the school in approximately 6 months time and will see your child then.

Should your child require routine dental care and is **not registered** with a family dentist or community clinic, please contact the *Designed to Smile* team on **02920 ******* who can help you find a dentist.

**PLEASE LET US KNOW IF YOU CHANGE ADDRESS BY CALLING THE DENTAL
TEAM ON 02920 *******

Seal or Varnish Missed Treatment Follow-up letter Version 2.0 – 29May2012

Appendix 40 Annual examination follow-up letter (parent guardian) (version 1.0)



Dear Parent/Guardian,

Your child's back teeth were examined by a dentist today as part of the Seal or Varnish study.

The outcome of the examination was:

- The dentist did not find anything during the examination that requires immediate attention. However if your child is registered with a dentist it is important to attend regularly.
- The dentist recommends that you make an appointment for your child to see a dentist for a more detailed examination **as further treatment may be necessary**. If your child is **not registered** with a family dentist or community clinic, please contact the *Designed to Smile* team on **02920 ******* who can help you find a dentist.

Seal or Varnish Annual Exam follow-up letter Version 1.0 - 12Jan2011

Appendix 41 Annual examination follow-up letter (dental practitioner) (version 1.0)

<<Insert date>>

Dear << insert name of General Dental Practitioner>>,

<<Insert name, address and date of birth of child>>

The above named child, whose parent or guardian has informed us is under your care, has been consented to participate in a randomised clinical trial, the aim of which is to determine the relative cost and effectiveness of fluoride varnish and fissure sealants in the prevention of dental caries in first permanent molars.

<<Insert name of child>> will be seen at six monthly intervals by the Community Dental Service when the mobile dental clinic visits their school to provide either the fluoride varnish or sealant treatment (depending on the arm of the study the child was allocated to). We have advised the child's parent or guardian that they should remain under your care. **However, if you would refrain from placing fissure sealants on first permanent molars or using topical fluoride treatments over the next 36 months that would be a great help in ensuring a valid outcome to the trial.**

If you have any queries regarding the trial, please contact us on the above telephone number. The study is being funded by the NHS Health Technology Assessment Programme, with the assent of the Chief Dental Officer and in collaboration with the South East Wales Trials Unit and the Dental Public Health Unit at Cardiff University Dental School.

Your co-operation in this matter will be very much appreciated.

Yours sincerely,



Ceri Hoddell

Senior Dental Officer & Principal Investigator

Cardiff and Vale University Health Board, Community Dental Service

01443 *****

Appendix 42 Letter to child's dentist withdrawal (version 1.0)

«Dentist_Name»

«Dentist_Address»

23rd October 2013

Dear «Dentist_Name»

«Child_First_Name» «Child_Surname», «Child_Address_1» «Child_Address_2», «Child_DOB»

I wrote to you on «Dentist_Letter_Sent_Date» informing you that the above child was enrolled in the Seal or Varnish clinical trial. The aim of the trial is to determine the relative cost and effectiveness of fluoride varnish and fissure sealants in the prevention of dental caries in first permanent molars. At that time, I asked if you would refrain from placing fissure sealants on first permanent molars or using topical fluoride treatments to ensure a valid outcome to the trial.

However «Withdrawal_Reason» *due to having moved to a school that is not involved in the study / at the request of his/her parent/*, «Child_First_Name» is no longer participating in the trial and there is therefore no longer any need for you to take any specific measures in *his / her* clinical management. We therefore return this child fully to your care.

If you have any queries regarding the trial, please contact us on the above telephone number. The study is being funded by the NHS Health Technology Assessment Programme, with the assent of the Chief Dental Officer and in collaboration with the South East Wales Trials Unit and the Dental Public Health Unit at Cardiff University Dental School.

Your co-operation in this matter is very much appreciated.

Yours sincerely,



Ceri Hoddell

Senior Dental Officer & Principal Investigator

Cardiff and Vale University Health Board, Community Dental Service

01443 *****

Appendix 43 Participant newsletter issue 1

Participants' Newsletter



SEAL OR VARNISH

Issue #1 - Autumn 2013

Hello from the Seal or Varnish study team!

We have had a fantastic response from children and their parents in the South Wales area over the last two years and are pleased to report that a final total of 1016 participants have entered the Seal or Varnish study. We would like to take this opportunity to thank you once again for your involvement and to provide an update as to where we currently are in the study and what upcoming events you can expect during the next 12 months.

Why 'Seal' or 'Varnish' children's teeth?

There are two treatments that dentists use to help prevent tooth decay in children's adult molar teeth. One is a fluoride 'varnish' which is painted on to the tooth (like fluoride toothpaste only stronger) that

Fluoride Varnish



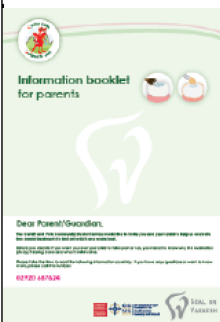
helps strengthen the tooth against decay. The second is a plastic coating (or 'sealant') to prevent the harmful bacteria that cause tooth decay collecting on the tooth surface.

Both treatments have been shown to work, and have been used for many years, however no one knows if one treatment is better than the other.

Plastic Sealant



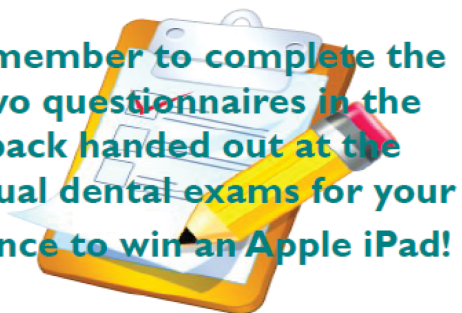
Information for parents



You will have received the Seal or Varnish 'Information booklet for parents' with your original invitation pack. If you would like us to send you another copy of the booklet, please call 02920 687624 or email us on: sealorvarnish@cardiff.ac.uk

iPad Competition!

Remember to complete the two questionnaires in the pack handed out at the annual dental exams for your chance to win an Apple iPad!



Seal or Varnish Newsletter Issue #1 - Autumn 2013



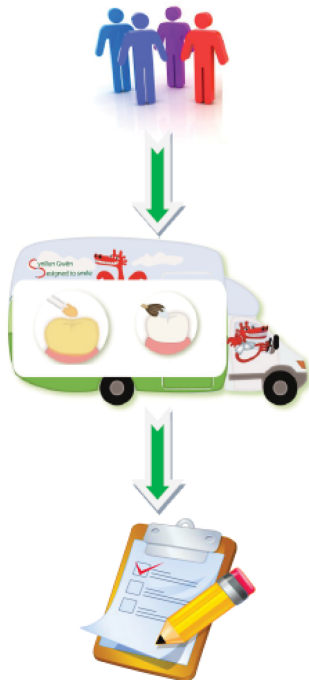
South East Wales
Trials Unit
Uned Ymchwil
De-ddwyrain Cymru



Any questions?
Please get in touch, we'd love to hear from you!

Cynllun Gwên
Designed to smile

STUDY FLOW CHART



Animals' teeth

Taking part in the Seal or Varnish study will help us learn more about how to look after our teeth, but have you thought about animals' teeth? Animals have teeth that come in all shapes and sizes and are used for doing different things.

Meat-eaters like lions (carnivores) have sharp teeth. Plant-eaters like horses (herbivores) have flat teeth. Animals which eat both meat and plants like monkeys and humans (omnivores) have a mixture of sharp teeth for tearing and flat teeth for grinding.

Here are some other interesting things about animals' teeth;

- While humans only have two sets of teeth in their lifetime, **sharks** lose teeth each week. They continually grow new teeth and may have over 20,000 teeth in their lifetime.
- **Crocodiles** have 60 teeth in their mouth but they too have lots of teeth in their lifetime – about 3,000.
- **Giraffes** have 32 teeth, just like humans.
- **Dolphins** have more teeth than any other animal – 200 in their mouth at the same time – imagine how long it would take to brush those! Scientists can tell the age of a dolphin by the rings on their teeth.



Dental Humour!

What did the dentist see at the North Pole?
.....A molar bear!



Meet the team: Some of the Community Dental Service staff and Mobile Dental Units used for the study

Upcoming
study activities

If you joined the study in 2011/2012 school year:

- September 2013 to January 2014: 24 month dental exams and treatment visits
- April 2014 to July 2014: 30 month treatment visits

If you joined the study in 2012/2013 school year:

- September 2013 to January 2014: 12 month dental exams and treatment visits
- April 2014 to July 2014: 18 month treatment visits

The Seal or Varnish Trial, South East Wales Trials Unit,
Institute of Translation, Innovation, Methodology & Engagement, Cardiff University School of Medicine,
7th Floor Neuadd Meirionnydd, Heath Park, Cardiff CF14 4YS

Seal or Varnish Newsletter Issue #1 - Autumn 2013



National Institute for
Health Research

Appendix 44 Participant newsletter issue 2

Participants' Newsletter



Issue #2 - Autumn 2014



Thank you for your ongoing participation!

A massive thank you for your continued participation in the Seal or Varnish study. This study will help inform and improve the health of children's teeth throughout Wales. We couldn't have done it without you!

Information for parents

This newsletter provides an update on the study so far.

Very soon you will be receiving a questionnaire pack from your child's school containing the **Dental Health Questionnaire** and the **Child Health Utility Questionnaire** with a pre-paid envelope. Now that your child is another year older, we would be extremely grateful if you could complete the appropriate questionnaire in order to update us on your child's usual dental routine and return these to us as soon as you can.

The more questionnaires we receive the stronger the findings will be ... **AND** as a thank you for returning the completed questionnaires, we will enter you into the **Apple iPad Prize Draw!**



Congratulations to the lucky winner at a Cardiff school who won the Apple iPad Prize last time!!



Interesting facts on types of teeth

Humans have two sets of teeth in their lifetime.

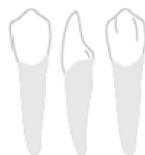
Primary teeth: We have 20 primary teeth, often called 'milk' teeth. The first tooth grows into the mouth between 6 months and 9 months old, although it can erupt earlier or later.

Permanent teeth: We have up to 32 permanent teeth. The front primary teeth become loose from about age 6 and fall out to allow the permanent teeth to grow into the space left behind. The last tooth doesn't come into the mouth until we are aged 18 to 21 years old. Unlike some other animals who have many different sets of teeth, or whose teeth keep on growing throughout life, humans only have one set of permanent teeth. They have to last for our whole lifetime.

Humans have three main types of teeth.



Incisors These are at the front of the mouth. They are flat in shape and are designed to incise or cut into food.



Canines Sometimes called 'eye' teeth, they are large and pointed. Humans have four of these—one on each side at the top and bottom of the mouth. These are designed for ripping and shredding our food.



Molars These are at the back of the mouth. They have a flattish surface and are designed for grinding and chewing our food.



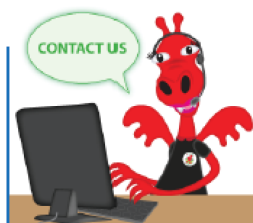
Joined the study in 2011 / 2012 school year?

Sept 2014—Jan 2015: Dental exam (36 month) and Questionnaire Pack
Feb 2015: End of study and return to normal dental care



Joined the study in 2012 / 2013 school year?

Sept 2014—Jan 2015: Dental exam, treatment visit (24 month) and Questionnaire Pack
Apr 2015—Jul 2015: Treatment visit (30 month)



Contact the Community Dental Service 'Seal or Varnish' Team
The Seal or Varnish Trial, Designed to Smile,
West 3A, Whitchurch Hospital, Cardiff, CF14 7XB
Phone: 02920 336 414 E-mail: designedtosmile.southwales@wales.nhs.uk



Appendix 45 Participant newsletter issue 3

Participants' Newsletter



Issue #3 - Autumn 2015



Thank you for participating in 2015!

Thank you once again for your continued participation in the Seal or Varnish study. This study will help inform and improve the health of children's teeth throughout Wales. We couldn't do it without you!

Information for parents

This autumn / winter we will complete the final assessment of your child's teeth.

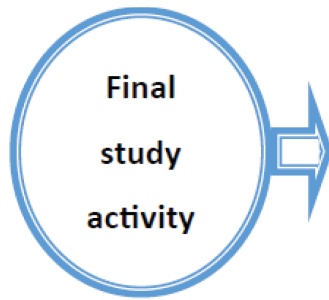
Very soon you will receive a questionnaire pack from your child's school containing the **Dental Health Questionnaire** and the **Child Health Utility Questionnaire** with a pre-paid envelope. This will be the last questionnaire pack that is sent to you. We would be extremely grateful if you could complete the appropriate questionnaire in order to update us on your child's usual dental routine and return these to us as soon as you can.

The more questionnaires we receive the stronger the findings will be ... AND as a thank you for returning your completed questionnaires for the final time, we will enter your child into the **Apple iPad Prize Draw!**

Congratulations!

Congratulations to the lucky winner in Rhondda Cynon Taff who won the Apple iPad Prize in May!!





Sept 2015—Jan 2016: Final dental assessment and last questionnaire Pack

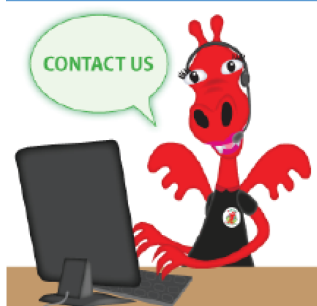
Feb 2016: End of study

Your child returns to their normal dental care

10 facts about teeth

Did you know...

1. The enamel on the top surface on your tooth is the hardest part of your entire body.
2. Your mouth produces over 25,000 litres of saliva in a lifetime—that's enough to fill two swimming pools. Saliva has many uses, including assisting you with your digestion and protects your teeth from bacteria in your mouth.
3. A snail's mouth is no larger than the head of a pin, but it can have over 25,000 teeth!!
4. The elephant grinds its molars and grows new ones. This happens six times in its lifetime. Its molar is about 7 inches square and can weigh over 6 pounds.
5. The Blue Whale is the largest mammal on earth, but it eats only tiny shrimp because it has no teeth.
6. The Crocodile Bird flies into the open mouth of a crocodile and cleans the crocodile's teeth.
7. Teeth start to form even before you are born—milk teeth or baby teeth start to form when the baby is in the womb, but they come through when the child is between 6–12 months old.
8. No two people have the same set of teeth—your teeth are as unique as your fingerprint, so be proud of your unique set of teeth.
9. One third of your tooth is underneath your gums—that means only two thirds of your tooth's length is visible.
10. In China, September 20th is an official holiday known as "Love Your Teeth Day".



Contact the Community Dental Service 'Seal or Varnish' Team

The Seal or Varnish Trial, Designed to Smile,

West 3A, Whitchurch Hospital, Cardiff, CF14 7XB

Phone: 02920 336 414 E-mail: designedtosmile.southwales@wales.nhs.uk



South East Wales
Trials Unit

Uned Ymchwil
De-ddwyrain Cymru



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