



Clinical trial results:

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

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2010-023476-23 |
| Trial protocol | GB |
| Global end of trial date | 21 December 2015 |

Results information

| | |
|-----------------------------------|---|
| Result version number | v1 (current) |
| This version publication date | 06 January 2019 |
| First version publication date | 06 January 2019 |
| Summary attachment (see zip file) | HTA Final report v2.0 (HTA 08.104.04 Final Report v 2.0 Clean.docx) Appendices (08_08_104_04 APPENDICES v2 CLEAN.docx) |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | SPON766-09 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|----------------|
| ISRCTN number | ISRCTN17029222 |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Cardiff University |
| Sponsor organisation address | 7th Floor, 30-36 Newport Road, Cardiff, United Kingdom, CF24 0DE |
| Public contact | Ivor Chestnutt, Cardiff University, 02920 746680, ChestnuttIG@cardiff.ac.uk |
| Scientific contact | Ivor Chestnutt, Cardiff University, 02920 746680, ChestnuttIG@cardiff.ac.uk |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 12 April 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 21 December 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective for this study was to:

To compare the clinical effectiveness of Pit and Fissure Sealants (PFS) and Fluoride Varnish (FV) in preventing dental caries in first permanent molars in 6-7 year-olds, as determined by:

- The proportion of children developing caries on any one of up to four treated first permanent molars
- The number of treated first permanent molar teeth caries-free at 36 months

Protection of trial subjects:

For participants receiving either the Pit and Fissure Sealant or Fluoride Varnish, preventing dental caries in their first permanent molar teeth outweighed the risk of the potential side effects from either treatment. FV application is not recommended in children with severe allergic tendencies (i.e. those who have previously been hospitalised for asthma). We actively sought out and excluded such children from the study.

Background therapy:

There is no background therapy used in this trial.

Evidence for comparator:

Pit and fissure sealants comprise a Bis-GMA resin, which is applied to the occlusal surface of the tooth using acid-etch technology. They work by physically obliterating the pit and fissure system which harbours cariogenic organisms and thereby inhibit the initiation of caries. First developed in the 1960s, they are an established technology and widely used in clinical practice. Numerous studies have investigated the clinical effectiveness of fissure sealants and this has been the subject of a recent Cochrane review. A meta-analysis of seven studies comparing sealed teeth to untreated controls demonstrated caries reductions ranging from 87% at 12 months to 60% at 48-54 months (Ahovuo-Saloranta et al., 2008).

Fluoride varnishes have also been marketed since the 1960s and comprise a topical medication which is painted onto the tooth surface. They contain a high concentration of fluoride (22,600 ppm) and are licensed for application by dental professionals. The varnish forms a quick-setting base which subsequently releases fluoride. Fluoride acts to prevent caries by inhibiting the demineralisation and encouraging the remineralisation of dental enamel. A Cochrane review suggested a pooled prevented fraction estimate of 46% (95%CI 30%-63%) when fluoride varnish is tested against no treatment controls (Marhino et al., 2002).

| | |
|---|--------------|
| Actual start date of recruitment | 07 July 2011 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|----------------------|
| Country: Number of subjects enrolled | United Kingdom: 1015 |
|--------------------------------------|----------------------|

| | |
|------------------------------------|------|
| Worldwide total number of subjects | 1015 |
| EEA total number of subjects | 1015 |

Notes:

| Subjects enrolled per age group | |
|---|------|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 1015 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from primary schools in 'Communities first' areas in South Wales as designated by the Welsh assembly government. Recruitment occurred between July 2011 and September 2012.

Pre-assignment

Screening details:

Invited participants who provided consent to participation were screened for adherence to inclusion/exclusion criteria through a returned medical history form and subsequently via baseline dental examination.

Pre-assignment period milestones

| | |
|--|-------------------------------------|
| Number of subjects started | 1406 ^[1] |
| Intermediate milestone: Number of subjects | Assessment of medical history: 1406 |
| Intermediate milestone: Number of subjects | Screening assessment: 1303 |
| Number of subjects completed | 1015 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|---------------------------------|
| Reason: Number of subjects | Consent withdrawn by subject: 2 |
| Reason: Number of subjects | Physician decision: 103 |
| Reason: Number of subjects | Deemed ineligible: 286 |

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Participants returned consent and medical history prior to assessment for inclusion in the trial. Only those that were deemed eligible were officially enrolled on the study.

Period 1

| | |
|------------------------------|----------------|
| Period 1 title | Baseline |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Varnish |

Arm description:

Participants allocated to this arm received 6 monthly treatments of fluoride varnish applied to first permanent molars included in the trial.

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Duraphat |
| Investigational medicinal product code | PL 00049/0042 |
| Other name | |
| Pharmaceutical forms | Dental suspension |
| Routes of administration | Dental use |

Dosage and administration details:

Fluoride varnish (FV) was supplied as 10 ml tubes (50 mg/ml dental suspension, equivalent to 22,600ppm fluoride) for multiple applications and applied topically as a thin layer to the pits, fissures and smooth surfaces of eligible teeth. As per the Duraphat Summary of Product Characteristics (SmPC), dosage per single application did not exceed 0.4 ml.

Initial application of FV will occur within 2 weeks of the baseline dental examination, and was

performed by a suitably qualified and trained dental hygienist according to the conventional clinical protocol established by the Community Dental Service. FV was re-applied at 6, 12, 18, 24, and 30 months (maximum of six applications).

| | |
|--|---|
| Arm title | Sealant |
| Arm description: | |
| Participants allocated to this arm received a pit and fissure sealant on the occlusal surface of any erupted first permanent moar included in the trial. | |
| Arm type | Non-IMP comparator |
| Investigational medicinal product name | Delton Light Curing Pit & Fissure Sealant |
| Investigational medicinal product code | CE0086 |
| Other name | |
| Pharmaceutical forms | Dental gel |
| Routes of administration | Dental use |

Dosage and administration details:

The Pit and Fissure Sealant (PFS) used for evaluation in the study was Delton Light Curing Opaque Pit & Fissure Sealant, which is the same PFS used in the current school based Designed to Smile programme. PFS will be supplied as 2.7 ml bottles for multiple applications and applied topically as a thin layer to occlusal surface of eligible teeth.

Initial application of PFS will occur within 2 weeks of the baseline dental examination, and will be performed by a suitably qualified and trained dental hygienist according to the conventional clinical protocol established by the Community Dental Service.

The condition of the PFS will be re-examined at 6, 12, 18, 24, and 30 months, and will be re-applied if the existing sealant has become detached, or if attachment is considered insufficient.

| Number of subjects in period 1 | Varnish | Sealant |
|---------------------------------------|---------|---------|
| Started | 501 | 514 |
| Completed | 501 | 514 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | 36 Months |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Assessor ^[2] |

Blinding implementation details:

Only dental assessors were blind to treatment allocation. Assessors did not have access to any of the treatment records or trial documentation in order to maintain their blind. However, it may have been possible for the assessors to identify those children treated with pit and fissure sealant as this would be apparent on inspection.

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|--|---|
| Arm title | Sealant |
| Arm description: - | |
| Arm type | Non-IMP comparator |
| Investigational medicinal product name | Delton Light Curing Pit & Fissure Sealant |
| Investigational medicinal product code | CE0086 |
| Other name | |
| Pharmaceutical forms | Dental gel |
| Routes of administration | Dental use |

Dosage and administration details:

The Pit and Fissure Sealant (PFS) used for evaluation in the study was Delton Light Curing Opaque Pit & Fissure Sealant, which is the same PFS used in the current school based Designed to Smile programme. PFS will be supplied as 2.7 ml bottles for multiple applications and applied topically as a thin layer to occlusal surface of eligible teeth.

Initial application of PFS will occur within 2 weeks of the baseline dental examination, and will be performed by a suitably qualified and trained dental hygienist according to the conventional clinical protocol established by the Community Dental Service.

The condition of the PFS will be re-examined at 6, 12, 18, 24, and 30 months, and will be re-applied if the existing sealant has become detached, or if attachment is considered insufficient.

| | |
|--|-------------------|
| Arm title | Varnish |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Duraphat |
| Investigational medicinal product code | PL 00049/0042 |
| Other name | |
| Pharmaceutical forms | Dental suspension |
| Routes of administration | Dental use |

Dosage and administration details:

Fluoride varnish (FV) was supplied as 10 ml tubes (50 mg/ml dental suspension, equivalent to 22,600ppm fluoride) for multiple applications and applied topically as a thin layer to the pits, fissures and smooth surfaces of eligible teeth. As per the Duraphat Summary of Product Characteristics (SmPC), dosage per single application did not exceed 0.4 ml.

Initial application of FV will occur within 2 weeks of the baseline dental examination, and was performed by a suitably qualified and trained dental hygienist according to the conventional clinical protocol established by the Community Dental Service. FV was re-applied at 6, 12, 18, 24, and 30 months (maximum of six applications).

Notes:

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: 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 examination at baseline, 12, 24 and 36 months was not informed of the arm to which the participant had been randomised. However, the presence or absence of fissure sealants at assessment would obviously indicate the likely treatment received.

| Number of subjects in period 2 | Sealant | Varnish |
|---------------------------------------|---------|---------|
| Started | 514 | 501 |
| 12 months | 484 | 474 |
| 24 months | 468 | 452 |
| 36 months | 418 | 417 |
| Completed | 418 | 417 |
| Not completed | 96 | 84 |
| Consent withdrawn by subject | 5 | 6 |

| | | |
|---|----|----|
| Missed final assessment (primary outcome) | - | 14 |
| Missed assessment (primary outcome) | 16 | - |
| Lost to follow-up | 75 | 64 |

Baseline characteristics

Reporting groups

| | |
|--|---------|
| Reporting group title | Varnish |
| Reporting group description: | |
| Participants allocated to this arm received 6 monthly treatments of fluoride varnish applied to first permanent mo;ars included in the trial. | |
| Reporting group title | Sealant |
| Reporting group description: | |
| Participants allocated to this arm received a pit and fissure sealant on the occlusal surface of any erupted first permanent moar included in the trial. | |

| Reporting group values | Varnish | Sealant | Total |
|--|---------|---------|-------|
| Number of subjects | 501 | 514 | 1015 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 501 | 514 | 1015 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 266 | 277 | 543 |
| Male | 235 | 237 | 472 |
| Number of children with dentine caries in the primary dentition (d4-6) | | | |
| This is the number of children at baseline who were assessed as having caries into dentine in their primary dentition (baby teeth) | | | |
| Units: Subjects | | | |
| Children with dentine caries | 266 | 286 | 552 |
| Children without dentine caries | 235 | 228 | 463 |
| Number of children with dentine caries in the primary dentition (d4-6mft) | | | |
| Number of children assessed as having dentine into caries in the primary dentition at the tooth level | | | |
| Units: Subjects | | | |
| Dentine caries in the primary dentition (d4-6mft) | 339 | 342 | 681 |
| No dentine caries in primary dentition (d4-6mft) | 162 | 172 | 334 |
| Children with untreated dentine caries in any First Permanent Molar (D4-6) | | | |
| The number of cihdren assessed as having untreated caries into dentine at the surface level on any one first permanent molar (FPM) | | | |
| Units: Subjects | | | |
| Untreated dentine caries on any FMP (D4-6) | 23 | 22 | 45 |

| | | | |
|--|-----|-----|-----|
| Without untreated dentine caries on any FMP (D4-6) | 478 | 492 | 970 |
| Children with dentine caries in any first permanent molar (D4-6MFT) | | | |
| Number of children assessed as having caries into dentine at the tooth level in any first permanent molar (FPM). | | | |
| Units: Subjects | | | |
| Dentine caries in any FPM (D4-6MFT) | 31 | 27 | 58 |
| Without dentine caries in any FPM (D4-6MFT) | 470 | 487 | 957 |

End points

End points reporting groups

| | |
|---|---------|
| Reporting group title | Varnish |
| Reporting group description: Participants allocated to this arm received 6 monthly treatments of fluoride varnish applied to first permanent molars included in the trial. | |
| Reporting group title | Sealant |
| Reporting group description: Participants allocated to this arm received a pit and fissure sealant on the occlusal surface of any erupted first permanent molar included in the trial. | |
| Reporting group title | Sealant |
| Reporting group description: - | |
| Reporting group title | Varnish |
| Reporting group description: - | |

Primary: Number of children developing dentine caries on any FPM

| | |
|--|---|
| End point title | Number of children developing dentine caries on any FPM |
| End point description: The proportion of children with dentine caries (D4-6MFT) on any FPM in the trial at 36 month examination | |
| End point type | Primary |
| End point timeframe: 36 months | |

| End point values | Sealant | Varnish | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 418 | 417 | | |
| Units: D4-6MFT | | | | |
| No dentinal caries on any first permanent molar | 336 | 344 | | |
| Dentine caries (D4-6MFT) on at least one FPM | 82 | 73 | | |

Statistical analyses

| | |
|----------------------------|-------------------|
| Statistical analysis title | Primary Outcome |
| Comparison groups | Sealant v Varnish |

| | |
|---|----------------------|
| Number of subjects included in analysis | 835 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 1.21 |
| Variability estimate | Standard deviation |

| | |
|---|---|
| Statistical analysis title | Primary Outcome (adjusted for school attended) |
| Comparison groups | Sealant v Varnish |
| Number of subjects included in analysis | 835 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 1.21 |
| Variability estimate | Standard deviation |

Secondary: Number of children developing dentine caries at 36 months by number of FPM in trial

| | |
|------------------------|---|
| End point title | Number of children developing dentine caries at 36 months by number of FPM in trial |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 36 months | |

| End point values | Sealant | Varnish | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 418 | 417 | | |
| Units: D4-6MFT | | | | |
| No caries on any FPM | 336 | 344 | | |
| Caries on 1 FPM | 53 | 43 | | |
| Caries on 2 FPM | 22 | 17 | | |
| Caries on 3 FPM | 5 | 9 | | |
| Caries on 4 FPM | 2 | 4 | | |

Statistical analyses

| Statistical analysis title | FPM with dentine caries, restoration or extraction |
|--|--|
| Statistical analysis description: | |
| Ordinal regression analysis of the number of FPM with dentine caries, a restoration or extracted but to caries (D4-6MFT) at 36 months by trial intervention arm. | |
| Comparison groups | Sealant v Varnish |
| Number of subjects included in analysis | 835 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | Ordinal Regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 1.2 |
| Variability estimate | Standard deviation |

Secondary: Number of surfaces with dentine caries per participant

| | |
|---|--|
| End point title | Number of surfaces with dentine caries per participant |
| End point description: | |
| The number of FPM surfaces per participant developing dentine caries at 36 months | |
| End point type | Secondary |
| End point timeframe: | |
| 36 months | |

| End point values | Sealant | Varnish | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 418 | 417 | | |
| Units: D4-6MFS | | | | |
| D4-6 MFS=0 | 336 | 344 | | |
| 1 with caries | 46 | 36 | | |
| 2 with caries | 14 | 17 | | |
| 3 with caries | 11 | 7 | | |
| 4 with caries | 3 | 6 | | |
| 5 with caries | 4 | 4 | | |
| 6 with caries | 1 | 1 | | |
| 7 with caries | 2 | 0 | | |
| 10 with caries | 1 | 0 | | |
| 20 with caries | 0 | 2 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Number of FPM surfaces with dentine caries |
| Statistical analysis description: | |
| Ordinal regression ananalysis of the number of FPM surfaces with dentine caries (D4-6MFS) at 36 months by trial arm | |
| Comparison groups | Sealant v Varnish |
| Number of subjects included in analysis | 835 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Ordinal Regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 1.19 |

Secondary: Association of treatment visits

| | |
|---|---------------------------------|
| End point title | Association of treatment visits |
| End point description: | |
| The number of treatment visits attended by each child who also underwent a final clinical examination at 36 months. | |
| End point type | Secondary |
| End point timeframe: | |
| 36 months | |

| End point values | Sealant | Varnish | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 418 | 417 | | |
| Units: Number of treatment visits | | | | |
| 1 treatment visit, No FPM with DMFT | 1 | 0 | | |
| 2 treatment visits, No FPM with DMFT | 0 | 0 | | |
| 3 treatment visits, No FPM with DMFT | 1 | 4 | | |
| 4 treatment visits, No FPM with DMFT | 13 | 11 | | |
| 5 treatment visits, No FPM with DMFT | 75 | 80 | | |
| 6 treatment visits, No FPM with DMFT | 246 | 249 | | |
| 1 treatment visit, at least one FPM with DMFT | 0 | 0 | | |
| 2 treatment visits, at least one FPM with DMFT | 0 | 1 | | |
| 3 treatment visits, at least one FPM with DMFT | 1 | 0 | | |
| 4 treatment visits, at least one FPM with DMFT | 3 | 4 | | |
| 5 treatment visits, at least one FPM with DMFT | 17 | 16 | | |
| 6 treatment visits, at least one FPM with DMFT | 61 | 52 | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Effects of treatment adherence |
| Statistical analysis description: | |
| To determine the effects of adherence to the scheduled number of treatment visits, a Complier Average Causal Effect analysis was conducted. As Fissure Sealant was the standard treatment in the Design to Smile program prior to the trial, this was assumed to be the control with treatment visits set to a constant (zero). | |
| Comparison groups | Sealant v Varnish |
| Number of subjects included in analysis | 835 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Complier Average Causal Effect |
| Parameter estimate | Efficacy coefficient |
| Point estimate | -0.005 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.014 |
| upper limit | 0.004 |

Secondary: Adherence to pre-specified treatment window

| | |
|------------------------|---|
| End point title | Adherence to pre-specified treatment window |
| End point description: | |

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 36 months | |

| End point values | Sealant | Varnish | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 418 | 417 | | |
| Units: Number of treatments outside window | | | | |
| 0 treatments outside window | 302 | 296 | | |
| 1 treatment outside window | 106 | 112 | | |
| 2 treatment outside window | 7 | 5 | | |
| 3 treatment outside window | 1 | 3 | | |
| 4 treatment outside window | 2 | 0 | | |
| 5 treatment outside window | 0 | 1 | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Effect of number of treatments outside of window |
| Statistical analysis description: | |
| To test for the effect of adherence to the treatment window, a binary indicator was added to the primary model which categorise the participants as having received: | |
| 1) All of their treatment visits within window | |
| 2) At least one visit out of window | |
| Comparison groups | Sealant v Varnish |
| Number of subjects included in analysis | 835 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.052 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.43 |
| upper limit | 1 |

Secondary: Enamel caries on any FPM in the trial

| | |
|---|---------------------------------------|
| End point title | Enamel caries on any FPM in the trial |
| End point description: | |
| The proportion of children with D1-6MFT (caries into enamel) on any FPM in the trial at 36 months | |
| End point type | Secondary |
| End point timeframe: | |
| 36 months | |

| End point values | Sealant | Varnish | | |
|------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 418 | 417 | | |
| Units: D1-6MFT | | | | |
| No caries on any FPM | 95 | 135 | | |
| Caries D1-6MFT on at least one FPM | 323 | 282 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Effect of treatment on caries in enamel |
| Comparison groups | Sealant v Varnish |
| Number of subjects included in analysis | 835 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.56 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.41 |
| upper limit | 0.78 |

Secondary: Whole mouth caries experience

| | |
|---|-------------------------------|
| End point title | Whole mouth caries experience |
| End point description: | |
| Total number of permanent teeth, per participant, affected by D4-6MFT | |
| End point type | Secondary |
| End point timeframe: | |
| 36 Months | |

| End point values | Sealant | Varnish | | |
|--------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 418 | 417 | | |
| Units: NUmber of teeth | | | | |
| 0 permanent teeth with D4-6MFT | 326 | 334 | | |
| 1 permanent teeth with D4-6MFT | 56 | 42 | | |
| 2 permanent teeth with D4-6MFT | 27 | 26 | | |

| | | | | |
|--------------------------------|---|----|--|--|
| 3 permanent teeth with D4-6MFT | 5 | 11 | | |
| 4 permanent teeth with D4-6MFT | 3 | 4 | | |
| 6 permanent teeth with D4-6MFT | 1 | 0 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Impact of trial treatment on all permanent teeth |
| Statistical analysis description: To examine the difference in the number of affected teeth Poisson and Binomial distribution modelling was carried out. | |
| Comparison groups | Sealant v Varnish |
| Number of subjects included in analysis | 835 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Poisson regression |
| Parameter estimate | Incident Rate Ratio |
| Point estimate | 0.94 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.74 |
| upper limit | 1.2 |

| | |
|---|--|
| Statistical analysis title | Copy of Impact of trial treatment on all perman... |
| Statistical analysis description: To examine the difference in the number of affected teeth Poisson and Binomial distribution modelling was carried out. | |
| Comparison groups | Sealant v Varnish |
| Number of subjects included in analysis | 835 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Negative Binomial regression |
| Parameter estimate | Incident Rate Ratio |
| Point estimate | 0.93 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.82 |
| upper limit | 1.46 |

| | |
|--|--|
| Statistical analysis title | Copy of Copy of Impact of trial treatment on al... |
| Statistical analysis description: To examine the difference in the number of affected teeth Poisson and Binomial distribution modelling | |

was carried out.

| | |
|---|----------------------------------|
| Comparison groups | Sealant v Varnish |
| Number of subjects included in analysis | 835 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Zero inflated poisson regression |
| Parameter estimate | Incident Rate Ratio |
| Point estimate | 1.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.76 |
| upper limit | 1.35 |

Statistical analysis title

Copy of Copy of Copy of Impact of trial treatme...

Statistical analysis description:

To examine the difference in the number of affected teeth Poisson and Binomial distribution modelling was carried out.

| | |
|---|---|
| Comparison groups | Sealant v Varnish |
| Number of subjects included in analysis | 835 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | 0 inflated negative binomial regression |
| Parameter estimate | Incident Rate Ratio |
| Point estimate | 1.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.75 |
| upper limit | 1.35 |

Secondary: Number of children developing dentine caries on any treated FPM at 12 months

| | |
|-----------------|--|
| End point title | Number of children developing dentine caries on any treated FPM at 12 months |
|-----------------|--|

End point description:

The proportion of children with caries (D4-6MFT) on any treated FPM in the trial at the 12 month annual examination

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

12 month examination

| End point values | Sealant | Varnish | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 450 | 444 | | |
| Units: D4-6MFT | | | | |
| No caries on any FPM | 414 | 407 | | |
| Caries on at least one FPM | 36 | 37 | | |

Statistical analyses

| Statistical analysis title | Proportion of children with caries |
|--|------------------------------------|
| Statistical analysis description: | |
| Proportion of children with caries (D4-6MFT) on any treated FPM at 12 months | |
| Comparison groups | Sealant v Varnish |
| Number of subjects included in analysis | 894 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.76 |
| upper limit | 1.21 |

Secondary: Number of children developing dentine caries on any treated FPM at 24 months

| | |
|------------------------|--|
| End point title | Number of children developing dentine caries on any treated FPM at 24 months |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 24 months | |

| End point values | Sealant | Varnish | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 439 | 424 | | |
| Units: D4-6MFT | | | | |
| No caries on any FPM | 378 | 361 | | |
| Caries on at least one FPM | 61 | 63 | | |

Statistical analyses

| | |
|--|------------------------------------|
| Statistical analysis title | Proportion of children with caries |
| Statistical analysis description: | |
| Proportion of children with caries (D4-6MFT) on any treated FPM at 24 months | |
| Comparison groups | Sealant v Varnish |
| Number of subjects included in analysis | 863 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.41 |
| upper limit | 2.62 |

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Adverse events were monitored from baseline treatment (0 months) until the final examination (36 months)

Adverse event reporting additional description:

No adverse events were reported in either arm for the duration of the trial.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Sealant |
|-----------------------|---------|

Reporting group description:

All participants randomised to receive Pit and Fissure Sealant

| | |
|-----------------------|---------|
| Reporting group title | Varnish |
|-----------------------|---------|

Reporting group description:

All participants randomised to receive fluoride varnish

| Serious adverse events | Sealant | Varnish | |
|---|-----------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 514 (0.00%) | 0 / 502 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Sealant | Varnish | |
|---|-----------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 514 (0.00%) | 0 / 502 (0.00%) | |

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: The treatments studied in this trial are licensed and well tolerated. No serious adverse events were reported

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|--|
| 18 July 2011 | Amendment included re-wording of primary objective as requested by ethics committee Change to timing of participant ID assignation Changes to methods of approach for data collection; use of home based questionnaires as opposed to telephone administration or via semi-structured questionnaires Revisions to frequency and of method of clinical, health economics and process evaluation assessments Clarification of adverse event assessment and adverse event reporting |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28613154>

<http://www.ncbi.nlm.nih.gov/pubmed/28394709>

<http://www.ncbi.nlm.nih.gov/pubmed/23167481>