The Effectiveness of Sealants in Managing Carious Lesions

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ABSTRACT

A barrier to providing sealants is concern about inadvertently sealing over caries. The objective of this meta-analysis was to examine whether sealants are effective in preventing caries progression.

Methods: Our search of electronic databases for comparative studies examining caries progression in sealed permanent teeth located 1905 unique records. We ordered 311 articles that met the inclusion criteria. We used a random-effects model to estimate percentage reduction in caries progression in sealed carious teeth compared to not-sealed carious teeth.

Findings: Six studies including 4 randomized-controlled trials (RCT) were used in the analysis (1090 surfaces, 840 teeth, and 384 persons). The median annual percentage of non-cavitated lesions progressing was 2.6% for sealed and 12.6% for unsealed carious teeth. The summary prevented fraction for RCT was 71.3% (95%CI: 52.8%-82.5%; no observed heterogeneity).

Conclusions: Sealing non-cavitated caries in permanent teeth reduces caries progression by over 70% up to 5 years after placement.

There is strong evidence that sealants are effective in both clinical and school settings for preventing caries in children at varying risk (Truman *et a*l., 2001; Ahovou-Saloranta *et al*., 2004). The evidence for sealant effectiveness in managing as opposed to preventing dental caries is limited, however. One review that examined the effectiveness of interventions to manage caries for the National Institutes of Health (NIH) Caries Consensus Conference included only 1 study on sealants (Bader *et al*., 2001). Despite the strong evidence of effectiveness, sealant prevalence among lower-income children (who are at higher risk for dental caries) is about 25% (Beltrán-Aguilar *et al.*, 2005), well below the Healthy People 2010 objective of 50%.

Survey data of dentists suggest that 1 of the major barriers to providing sealants is concern about inadvertently sealing over caries (Chapko, 1987; Primosch and Barr, 2001). This concern has also been a barrier to implementing school-based sealant programs (Association of State and Territorial Dental Directors, unpublished data, 2005)

Documenting the effectiveness of sealants in managing existing caries is therefore important and such documentation could potentially remove barriers to providing a proven intervention. The purpose of this systematic review is to examine the effectiveness of dental sealants in preventing the progression of carious lesions in the pits and fissures of permanent teeth.

METHODS

Inclusion Criteria

We included studies published in English that compared caries progression in known carious lesions in permanent teeth *in vivo* that received sealants with progression in unsealed teeth.

Identification of Studies

Our search of MEDLINE (1966 to June 2005) using a modified version of the strategy used by the NIH Caries Consensus Conference (University of Michigan, 2003) identified 1872 records. The MEDLINE search strategy was adapted to search EMBASE (1980 to June 2005), which identified 71 records and the Cochrane Central Register of Controlled Trials (accessed first week of September 2005), which identified 79 records. In total, there were 1905 unique records. Two reviewers independently examined the titles and abstracts of these records for systematic or narrative reviews of the effectiveness of sealants in preventing or managing caries and primary studies on managing caries. Because this analysis was part of a larger study that analyzed the effect of sealants on caries progression and bacteria levels, at this stage we screened the search results for studies with before-after or concurrent controls that examined outcomes on caries or bacteria activity in sealed carious lesions.

We ordered 262 articles: from our examination of their references, we ordered an additional 49 articles, for a total of 311.

Study Selection

One investigator (SG) screened all ordered articles and identified 31 potential qualifying studies. After these studies were reviewed by three investigators (BG, SG, and WK), consensus was reached that 26 studies should be abstracted. Of the 10 studies that examined the percentage of carious lesions progressing, 6 had concurrent controls.

Data Abstraction and Quality Assessment

Two reviewers (SG and EO) abstracted studies using a slightly modified version of a form developed for the NIH Caries Consensus Conference. The abstraction forms were jointly reviewed by 3 investigators (BG, SG, and EO) to assess study quality using criteria established by the third US Preventive Services Task Force (USPSTF; Harris *et al*., 2001). Studies were rated as "good" if they satisfied all criteria, "fair" if they did not satisfy each criterion but reviewers did not identify a methodologic flaw that invalidated the results, and "poor" if reviewers judged a methodologic flaw or flaws that likely invalidated the results.

Outcome and Effect Measures

Our outcome measure was the percentage of carious lesions progressing where progression was defined as demineralization or loss of tooth structure. To measure effectiveness we calculated the relative risk ratio (RR)

$$RR = \frac{\%\ \text{lesions progressing}_{\text{SEALED}}}{\%\ \text{lesions progressing}_{\text{NOT SEALED}}}$$

and its 95% confidence interval (CI). The prevented fraction can be obtained by subtracting the RR from 1 and the upper/lower 95% CI can be obtained by subtracting the lower/higher 95% CI of the RR ratio from 1.

Synthesis of Findings

We calculated the median percentage of lesions progressing in sealed and unsealed surfaces as well as the median prevented fraction for all studies and for subgroups of studies with selected characteristics (e.g., type of sealant material, baseline caries severity, and time to follow-up). We classified baseline caries as non-cavitated if the study described caries as incipient or restricted to the enamel or if there was no apparent defect in the enamel or lesion did not permit

explorer penetration. We classified caries as cavitated if the study stated that cavitation was visually detectible or the lesion allowed explorer penetration.

To obtain a weighted average of the RR and its 95% confidence interval, we used the DerSimonian and Laird (DSL) random effects model (Normand, 1999). We tested for homogeneity of effect size using the quantity I^2 (Higgins et al., 2003).

Addressing Limitations in Study Design and Data Reporting

In 2 studies, controls consisted of children who did not return permission slips, which may have introduced selection bias. To address the issue of non-randomization, we calculated the DSL summary effect measure for all studies and for those with random assignment.

Five studies did not conduct their analysis at the person level; of these, 3 used teeth and 2 employed surfaces as the unit of analysis. None of these studies adjusted for correlation among surfaces in the same tooth (intra-tooth) or correlation among teeth in the same patient (intra-patient). As intra-tooth or intra-patient correlation increases, the reported n in studies with multiple teeth (tooth pairs in split-mouth trials) or multiple surfaces is too high, and thus the standard error estimated with the reported n is too low. To address intra-tooth correlation, we adjusted the reported n assuming perfect correlation among tooth surfaces in 1 study (Gibson and Richardson, 1980) and in the other study we adjusted the number of surfaces using a correlation coefficient for pit and fissure surfaces that was calculated from data provided in the study (Heller et al., 1995). To address intra-patient correlation, we adjusted the number of teeth assuming no (0%), perfect (100%), and 30% correlation (30% value obtained from authors' analysis of data from the 1999-2004 National Health and Nutrition Examination Survey). A description of how we adjusted data and derived the correlation estimate of 30% is provided in the Web-Appendix).

Two studies, which were originally randomized split-mouth trials that sealed both sound and carious teeth, performed a sub-analysis of caries progression in treatment and control teeth that were carious at baseline, but the teeth in the sub-analysis were not necessarily paired data at the patient level. We assumed parallel comparison groups in these studies, which would over-estimate the standard error if most data were in fact paired (Web-Appendix).

In 2 studies, progression rates were extreme (either 0% in treatment or 100% in controls). To calculate the DSL summary RR, we adjusted extreme rates using the LaPlace procedure (Lewis and Sauro, 2006), which adds 1 to the number of successes (carious lesions progressing) and 2 to the number of trials (number of carious lesions).

Finally, for studies reporting the number of teeth but not the number of children in the treatment and control groups, we estimated the number of children using assumptions described in the footnotes to Figure 1.

RESULTS

Quality of Studies

The 6 studies with concurrent controls included in this analysis (Heller *et al*., 1995; Frenken *et al*., 1998; Florio *et al*., 2001; Gibson and Richardson, 1989; Going *et al*., 1976; and Mertz-Fairhurst *et al*., 1986, which together represented an estimated 384 persons, 840 teeth and 1090 surfaces) varied in terms of execution and design, baseline caries severity, and type of sealant material (Table 1). Four studies primarily sealed non-cavitated lesions, 1 exclusively sealed cavitated lesions, and 1 sealed both cavitated and non-cavitated lesions. If we assume that all teeth in the last study are cavitated, then 13.5% of carious teeth used in this analysis would be cavitated. Three studies used 2nd or 3rd generation resin-based sealants, 2 used glass ionomer cement (GIC), and 1 used 1st generation resin-based sealants. Study populations included children, adolescents, and young adults. All the studies were rated as "fair" quality (Table 2).

Effect of Sealants

The median annualized progression rates for sealed and unsealed lesions were respectively, 5.0% and 16.1% (Table 3). For non-cavitated lesions, these values were 2.6% and 12.6%, respectively, and for cavitated lesions, they were 19.4% and 59.3%.

For the individual studies, the prevented fraction ranged from 61.6% to 100.0% with a median of 74.2% (Table 3). Our subgroup analyses indicated that the median prevented fraction did not vary greatly by grouping, ranging from 61.6% for the study using 1st generation resin-based material to 87.7% calculated from the annualized values of the studies using GIC. Although there was some variation by type of sealant material and cavitation status, the median value always exceeded 50% (Table 3).

The RR for the studies ranged from 0 to 38.4%, but after adjusting the progression rate for extreme values, it ranged from 20.8% to 53.2% (Figure 1). The CI for each study widened as we made more conservative assumptions about correlation among teeth (Figure 1) but changing the assumptions about correlation did not result in rejecting findings of statistical significance for any of the 4 studies whose initial 95% CI did not contain 100%.

The summary DSL prevented fraction (calculated from the summary DSL RR) ranged from 73.2% (95% CI: 59.8%-82.2%) assuming perfect correlation among teeth (adjusted n=398) to 75.0% (95%CI: 67.1%-81.1%) assuming no correlation (adjusted n=946) and equaled 74.1% (95%CI: 63.8%-81.4%) assuming 30% correlation (adjusted n=638). When we restricted the analysis to the 4 randomized trials, the summary prevented fraction ranged from 71.2% (95%CI: 50.3%-83.3%) assuming perfect correlation (adjusted n=154) to 71.3% (95%CI: 54.1%-82.0%) assuming no correlation (adjusted n=254) and equaled 71.3% (95%CI: 52.8%-82.5%) assuming 30% correlation (adjusted n=207). The quantity I^2 was 0 regardless of our assumptions about correlation among teeth or whether to include only randomized trials, which indicates no observed heterogeneity.

DISCUSSION

We found that sealing carious lesions reduced the probability of lesion progression by more than 70%, an effect that was consistent across studies and robust. Neither changing assumptions about intra-patient correlation nor omitting non-randomized studies significantly affected the prevented fraction. The lower bound on the 95% CI always exceeded 50.0%.

The evidence supporting sealing non-cavitated lesions was strong, as these lesions accounted for almost 90% of teeth in this study, and their median annualized probability of progression was very low (2.6%). These findings do not support reported concerns about poorer outcomes associated with inadvertently sealing caries and should lessen the reluctance of practitioners to provide sealants -- an intervention proven to be highly effective in preventing caries. The annualized probability reflects progression in lesions recognized as "early or incipient" and suggests that the probability of progression for pit-and-fissure surfaces with caries considered "questionable" could be even lower. These findings not only support the placement of sealants to manage and arrest lesions determined to be in the early carious stages, but, just as importantly, support their placement for surfaces where caries status is uncertain.

Another notable finding of this review was the low annualized probability of progression (12.6%) for untreated, non-cavitated lesions. This finding suggests that immediate surgical treatment of such lesions may not be necessary. Thus, practitioners can consider sealing them or simply waiting and watching these lesions for signs of active progression. Applying sealants is particularly attractive, however, because the probability that a sealed non-cavitated lesion will not progress is per our study, 97% per year (or 3% per year that it will progress). Approaches focusing on prevention and management could potentially preserve tooth structure and lower the likelihood of complex restorations in future years.

This systematic review found considerable variation in sealant materials used, study designs, duration of the studies, and how caries progression was assessed. All studies were assigned a quality score of fair. One limitation of all but 1 study was how they assessed caries progression. Three studies assessed progression with a visual-tactile exam. In the absence of sealant loss or a restoration on a previously sealed carious lesion, visual-tactile assessment of caries under sealants is limited. In 1 of these studies, however, children received regular restorative care and thus it is likely that sealed teeth were periodically assessed radiographically and restored if necessary. In 3 of the studies, it appears that the baseline and follow-up exams were conducted by the same unblinded examiner. Blinding, however, is likely not possible unless sealants are removed at the follow-up exam.

This review did not find a difference between the effectiveness of GIC and resin-based sealant materials. Limited evidence exists to support the effectiveness of GIC sealant material as a primary preventive measure (Ahouvo-Saloranta *et. al*., 2004). In this review, the 2 studies examining GIC material differed from those using resin-based material in that they restricted their analysis to primarily non-cavitated lesions. Also, 1 of these 2 studies used resin-modified glass ionomer cement, which may have better retention.

Additional studies that meet current standards of quality in design and conduct are needed to build the evidence related to the effectiveness of sealants in preventing caries progression in cavitated lesions as well as their effectiveness relative to placing a restoration. Uniform criteria to assess progression from early demineralization to frank cavitation as well as standardized methodologies to measure progression are needed. This review would have been strengthened if all studies had used examiners calibrated to the same criteria to assess caries

progression and if all studies had used the same method to assess caries (i.e., visual-tactile exam with removal of sealants at follow-up exam).

In conclusion, the evidence supports placing sealants over non-cavitated carious lesions in the pits and fissures of permanent teeth in children, adolescents, and young adults. Our meta-analysis of 4 randomized controlled trials involving primarily sealed non-cavitated carious lesions found that the percentage reduction in caries progression in sealed lesions relative to not-sealed lesions was 71.3% (95% CI: 52.8% - 82.5%). Because at most 14% of carious teeth in this analysis could be classified as cavitated, we found insufficient evidence to make a recommendation for or against sealant placement on cavitated carious lesions.

Table1. Description of Studies Whose Data Was Used to Calculate Summary Measures

Study[a]	Subjects[b]	Sealants[c]	Study quality[d]
Florio; 2001; Brazil; 12	6-year-olds; prophylaxis every 3 months; NC[e]	Resin-modified GIC; No; 65.5%	23; 72; NA[f]; RCT[g] (parallel groups); 1year DO=9%; Direct digital radiography; NR[h]; NR
Frenken 1998; Zimbabwe; 36	Secondary school students (mean age=13.9 years); NR; NC	GIC; No; 20.4%	NR; 511 in sealed group (# controls NR); NA; Prospective cohort (parallel groups); 3year DO for sealed group=38.6%; VT[i]; Yes; NR
Gibson; 1980; Canada; 30	2nd graders; NR; NC	RB2[j]; NR; NR	NR; at follow-up -79; 111; Subgroup of RCT (originally designed as split-mouth design but in this analysis, control and treatment teeth not necessarily in same child); NR; VT exam and radiograph; NA; NR
Going[k]; 1976; United States; 12	10- to 14-year-olds; no fluoridation; NC/C	RB1; Yes[l]; NR	NR; 85 (first follow-up); NA; Subgroup of RCT (originally designed as split-mouth design but in this analysis, control and treatment teeth not necessarily in same child); Year 1 to Year 2 DO=21.1%; VT; NR; Yes

[a] First author; year published; country where conducted; duration (months)
[b] Age range; background prevention exposure; baseline caries severity
[c] Material; sealants maintained/repaired; retention rate
[d] Number of subjects at baseline; number of teeth; number of sites; design; drop-out rate for teeth (DO); how caries progression measured; examiner calibration; examiner blinding
[e] NC=non-cavitated and C=cavitated
[f] NA=not applicable.
[g] RCT=randomized controlled trial.
[h] NR= not reported.
[i] VT=visual-tactile examination.
[j] RB1 Resin-based-UV light polymerized; RB2 Resin-based-autopolymerized; RB3 Resin-based-light polymericed
[k] This was the only study that reported effectiveness for multiple follow-ups. We used the first-year results because Going used NuvaSeal, which may have lower retention rates than currently used sealant materials.
[l] For sealed teeth, year 1 findings reported for teeth retaining their sealant.

Heller; 1995; United States; 60	1st graders; fluoridation; NC	RB3; Yes; NR	71; NR; 436 surfaces (approximately 2 surfaces per tooth); NA; Retrospective cohort (parallel groups); NR; VT; NA; No
Mertz-Fairhurst; 1986; United States; 12	9 to 19 years; NR: C	RB2; NR; NR	20; 40; NA; RCT (split-mouth design); 1year DO=30%; Bodecker device; NR; Yes

Table 2: Quality Assessment of Six Studies with Concurrent Controls

CRITERIA	STUDY **Florio**	**Frenken**	**Gibson**	**Going**	**Heller**	**MF 86**
Initial assembly of comparable groups	Good – RCT[a]	Fair – assignment based on returned permission slip	Good – RCT	Good – RCT	Good – although assignment based on return permission slip, study used logistic regression to control for potential confounders	Good – RCT
Reliability and validity of measure of outcome	Fair - blinding not specified and whether same examiner at BL and FU indeterminate	Fair - VT[b] and sealants not removed at FU[c]; outside examiner	Fair - no blinding and same examiner at BL[d] and FU	Fair – VT and sealants not removed at FU	Fair - no blinding, same examiner at BL and FU, and VT where sealants not removed at FU although subjects received regular clinical care	Good-removed sealant and blinded examiners assessed lesion progression
No differential loss to FU or overall high loss to FU	Good – drop out rate was 9%.	Fair – number of controls not reported	Fair - drop out rates not reported	Fair – 1-year drop-out rate not reported	Fair – retrospective cohort study so drop out rate not reported	Fair – 1- year drop-out rate was 30%
Other threats to validity:	Fair – small sample size	None apparent	None apparent	None apparent	None apparent	Fair – small sample size

[a] RCT = randomized controlled trial.
[b] VT = visual tactile exam.
[c] FU = follow-up exam.
[d] BL = baseline exam.

QUALITY SCORE	Fair	Fair	Fair	Fair	Fair	Fair

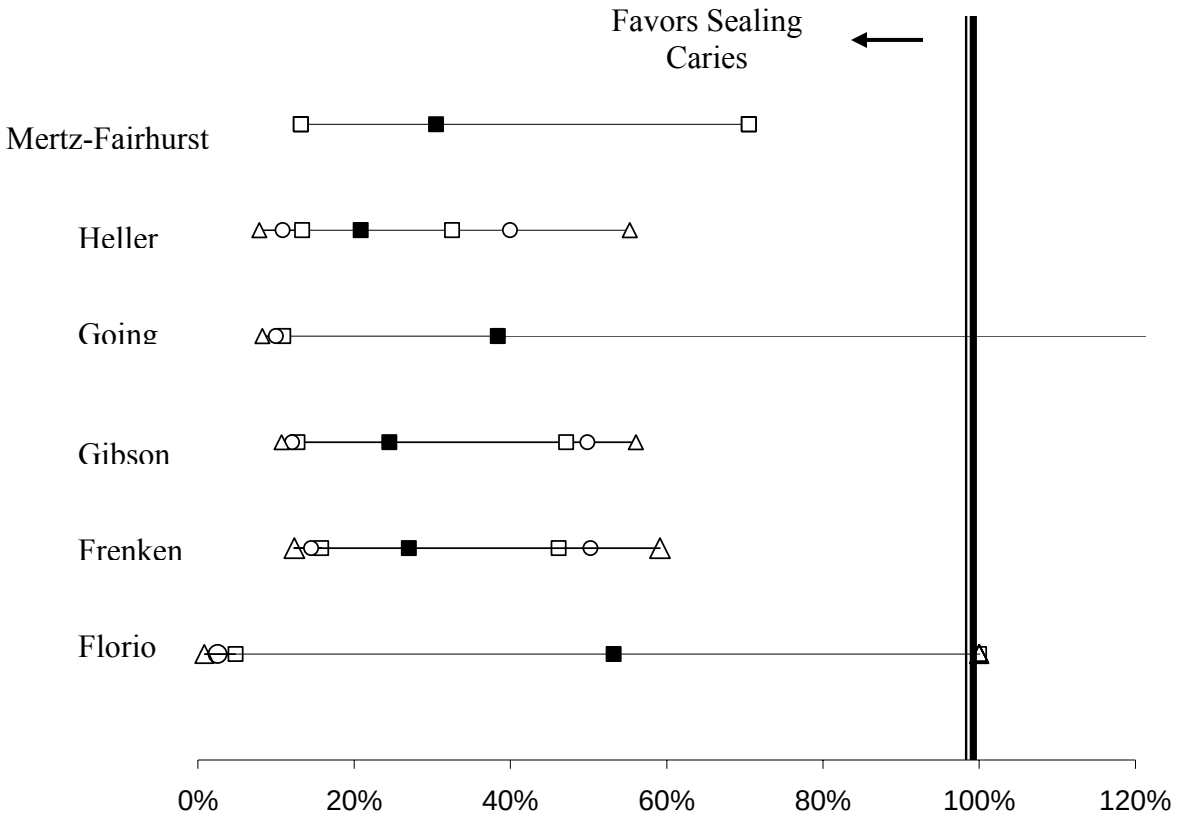
Table 3: Percentage of Sealed and Unsealed Carious Lesions Progressing and Prevented Fraction for Different Subgroups

	No. teeth	No. subjects	No. studies	Sealed Carious Lesions (%)		Unsealed Carious Lesions (%)		Prevented Fraction (%)	
				Median[a]	Range	Median	Range	Median	Range
All	840	384	6	9.6	0-28.6	41.4	6.1-100	74.2	61.6-100
RCT[b]	254	140	4	13.1	0.0-28.6	48.0	6.1-100	73.5	61.6-100
<=12 months	175	91	3	7.1	0-28.6	18.6	6.1-100	71.4	61.6-100
30 to 36 months	447	222	2	13.7	8.4-19.0	54.2	31.1-77.4	74.2	73.0-75.5
60 months	218	71	1	10.8	--	51.8	--	79.2	--
GIC[c]	430	193	2	4.2	0-8.4	18.6	6.1-31.1	86.5	73.0-100
RB1[d]	85	57	1	7.1	--	18.6	--	61.6	--
RB2[e]&RB3[f]	225	134	3	19.0	10.8-28.6	77.4	51.8-100	75.5	71.4-79.2
Non-cavitated	727	313	4	9.6	0-19.0	41.4	6.1-51.8	77.3	73.0-100
Cavitated	113	71	2	17.9	7.1-28.6	59.3	18.6-100	66.5	61.6-71.4
Annualized[g]									
All	840	384	6	5.0	0-31.7	16.1	6.1-100	78.7	68.3-100
RCT	254	140	4	7.6	0-31.7	31.7	6.1-100	75.2	68.3-100
GIC	430	193	2	1.4	0-2.9	8.9	6.1-11.7	87.7	75.3-100
RBI	85	57	1	7.1	--	18.6	--	61.6	--
RB2 &RB3	225	134	3	8.1	2.3-31.7	44.8	13.6-100	82.0	68.3-83.4
Non-cavitated	727	313	4	2.6	0-8.1	12.6	6.1-44.8	82.7	75.3-100
Cavitated	113	71	2	19.4	7.1-31.7	59.3	18.6-100	65.0	61.6-68.3

[a] In most cases mean was fairly close to median value.
[b] Randomized controlled trial.
[c] Glass ionomer cement sealants.
[d] 1st generation resin based sealants (UV light-polymerizing)
[e] 2nd generation resin-based sealants (auto-polymerizing).
[f] 3rd generation resin-based sealants (light-polymerizing)

[g]Reported values annualized assuming a constant progression rate (PR). Annualized % progressing $= 1 - (1 - (PR)^{\frac{1}{n}})$, where n represents years since placement

Figure 1 Adjusted relative risk ratios[a] and 95% confidence interval assuming 0, 30%, and 100% correlation among teeth



Florio values calculated adjusting extreme values with LaPlace procedure; progression rate of 0% in treatment group set to 3.2%, which resulted in adjusting relative risk ratio upward from 0.00% to 53.2%.

Frenken reported 569 students were screened at baseline and that the program delivered 368 sealants and thus the ratio of children to sealants was greater than 1. The study also reported restoring 307 teeth in 144 children (2.13 per child). We assumed 2.13 sealants were delivered per child.

Gibson was a split-mouth trial that sealed both carious and sound teeth, 1 to 2 tooth pairs per child. Study reported sealing 425 pairs of molars in 266 children, or 1.6 tooth pairs per child. We assumed half of sealed teeth were carious or 1.6 carious teeth per child. We also scaled the number of teeth by 79/111 because the analysis for carious teeth was conducted among 111 surfaces in 79 teeth.

For Going, another sub-analysis of this same study population took bacteria samples from 33 teeth in 22 children. We assumed 1.49 teeth per child.

Mertz-Fairhurst values calculated adjusting extreme values with LaPlace procedure; progression rate of 100% in control group set to 93.8%, which resulted in adjusting relative risk ratio upward from 28.6% to 30.5%.

[a] Progression rates of 0% or 100% adjusted using LaPlace procedure as described in text.

Figure 1 Legend

■ Relative risk ratio

□ 95% confidence interval assuming no correlation (rho=0.0)

○ 95% confidence interval assuming rho =0.3

Δ 95% confidence interval assuming rho=1.0.

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Web Appendix

Obtaining Effective Sample Size

Adjusting data for correlation among teeth

The effective sample size is defined as

$$n^* = \frac{p(1-p)}{v} \quad (1),$$

where v represents the variance of a sample proportion $\hat{p}$ under the complex design, and p represents the probability of a carious lesion progressing. Note that in the case when $\hat{p}$ is formed from independent observations, effective sample size coincides with the reported sample size n. Assume that for k children, teeth within each child are correlated with coefficient of correlation ρ but independent between the children, the formula for v is

$$Var(\hat{p}) = \frac{1}{n} p(1-p)\left(1 + \frac{\rho}{n}\sum_{j=1}^{k} m_j(m_j - 1)\right) \quad (2)^{a},$$

where m_j is the number of teeth from the child j. Summing m_j over j will yield n.

We assumed that for a given study each child had the same number of teeth examined. Letting m represent the number of teeth per child, the reported sample size, n, would equal km and (2) simplifies to

$$Var(\hat{p}) = \frac{1}{n} p(1-p)\big(1 + \rho(m-1)\big). \quad (3)$$

Substituting (3) into (1), we obtain

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[a] Sketch of the Proof: Assume n possibly correlated Bernoulli trials with probability p and outcomes Y_i. Proportion of successes over n trials $= \hat{p} = \frac{X}{n} = \frac{Y_1 + Y_2 + \cdots + Y_n}{n}$, with the variance $Var(\frac{X}{n}) = \frac{1}{n^2}\sum_{i=1}^{n} Var(Y_i) + \frac{1}{n^2}\sum_{i \neq j} Cov(Y_i Y_j)$, where $Var(Y_i) = p(1-p)$, and $Cov(Y_1, Y_2) = p(1-p)\rho$. Since there are $\sum_{j=1}^{k} m_j(m_j - 1)$ nonzero and identical covariances, (2) follows.

$$n^* = \frac{n}{1+\rho(m-1)}.$$

To estimate a common ρ, we used data from the National Health and Nutrition Examination Survey 1999-2004. This estimated value was 0.3 (0.2995 ± 0.0254) The effective sample sizes, n*, estimated for each study, which were in turn used to estimate the random effects summary measure, are provided in Table 1.

Table 1: Estimated effective sample size (after controlling for intra-mouth correlation) for each study included to calculate random effects relative risk ratio.

	Sealed				Not sealed			
Study	**k**	**n**	**M=n/k**	**n***	**k**	**n**	**m=n/k**	**n***
Florio	10	33	3.3	20	10	29	2.9	18
Frenken[4]	25	54	2.1	40	147	314	2.1	234
Gibson[5]	24	38	1.6	32	26	41	1.6	35
Going[6]	29	43	1.5	37	28	42	1.5	37
Heller[7]	63	282	4.5	138	8	42	5.2	18
Mertz-Fairhurst[8]	14	14	1	14	14	14	1.0	14

Section 2: Estimating correlation among the teeth

We used data from the National Health and Nutrition Examination Survey 1999-2004 to calculate the number of decayed and filled surfaces for each unsealed posterior permanent tooth among children aged 10 to 17 years. We then calculated the correlation matrix for the posterior teeth.

Table 2: Correlation Matrix

	Upper right quadrant				Upper left quadrant				Lower left quadrant				Lower right quadrant			
	2M	1M	2B	1B	1B	2B	1M	2M	2M	1M	2B	1B	1B	2B	1M	2M
2M	1	0.35	0.25	0.25	0.20	0.20	0.31	0.53	0.42	0.28	0.20	0.20	0.14	0.23	0.30	0.45
1M		1	0.30	0.28	0.21	0.19	0.65	0.37	0.34	0.52	0.20	0.20	0.21	0.24	0.49	0.34
2B			1	0.57	0.37	0.42	0.23	0.29	0.27	0.23	0.31	0.28	0.27	0.34	0.26	0.32
1B				1	0.51	0.37	0.24	0.27	0.32	0.25	0.38	0.32	0.37	0.32	0.28	0.31
1B					1	0.49	0.20	0.23	0.25	0.20	0.21	0.30	0.25	0.26	0.20	0.28
2B						1	0.21	0.26	0.27	0.18	0.26	0.24	0.13	0.27	0.21	0.27
1M							1	0.38	0.33	0.54	0.19	0.18	0.18	0.20	0.51	0.32
2M								1	0.48	0.30	0.27	0.21	0.14	0.26	0.31	0.43
2M									1	0.43	0.27	0.22	0.21	0.26	0.39	0.63
1M										1	0.23	0.20	0.20	0.26	0.64	0.37
2B											1	0.38	0.25	0.33	0.18	0.22
1B												1	0.50	0.35	0.18	0.19
1B													1	0.42	0.18	0.17
2B														1	0.27	0.28
1M															1	0.41
2M																1

We used a Fisher Z transformation to normalize the correlations. We then estimated the mean correlation, 0.305, and the 95% confidence interval (0.283 - 0.326)

Section 3: Adjusting Data for Different Study Design (Split-Mouth versus Parallel Comparison Groups)

If we were to misclassify paired data as independent data it is likely that we would overestimate the study variance. Recall that the formula for the variance of the log of the relative risk ratio is $Var(\ln(\hat{RR})) = Var(\ln(p_T)) + Var(\ln(p_c)) - 2Cov(\ln(p_c), \ln(p_T))$, where p_C and p_T respectively represent the probability of caries in the control and treatment groups[a]. If the treatment and control groups are paired, the covariance will likely be positive and thus larger than the variance for paired data. Indeed, the nonnegative covariance is subtracted from the sum of variances $Var(\ln(p_T)) + Var(\ln(p_C))$, which equals the variance for uncorrelated treatment and control data.

[a] Veth M, Poulsen S (1998). Comments on a commentary: statistical evaluation of split mouth caries trials. *Community Dent Oral Epidemiol* 26:80-3.