The logic behind the use of fissure sealant retention as a proxy outcome measure for dental caries prevention

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(Received June 25, 2016; Accepted September 7, 2016)

Abstract: Fissure sealant retention is traditionally considered as a proxy measure for caries prevention. This study investigated the logic behind this proposition, and its validity. A logical framework of the proposition was established. The mechanism of caries development was transferred into a Directed acyclic graph, and this was used to investigate the logical framework. The sensitivity and specificity of full sealant retention in the prediction of dental carious lesion development and the number of false positive/false negative prediction rates were computed. The sensitivity/specificity was statistically compared to that of random values. A contradiction in the logical framework was identified. The mean sensitivity/specificity was 37.9% (SD = 27.8%) and 67.6% (SD = 28.4%), respectively. When these values were compared against random values (30.5%, SD = 25.7% and 58.7%, SD = 31.6%), a non-significant sensitivity ($P = 0.06$) and a borderline higher specificity ($P = 0.04$) were observed. The overall false prediction rate was 33.7%, with 16.9% and 16.8% false negative and false positive predictions, respectively. The sensitivity/specificity was too low and the false prediction rate was too high to consider retention a valid proxy for caries prevention. The logic behind the investigated proposition is flawed, contradicted by the current empirical evidence, and thus invalid.

Keywords: formal logic; fissure sealant; predictive accuracy; reductio ad absurdum.

Introduction

Fissure sealants have been established as clinically (1) and financially effective (2,3) interventions for the prevention of caries development in dental pits and fissures.

The retention of the sealant material in dental pits and fissures is traditionally considered as a proxy measure for caries prevention (4) and, thus, is widely regarded as the single most important outcome measure for the evaluation of fissure sealant success (5). Moreover, a simple literature search in PubMed (Search date 29 December 2015, Additional S1 File) revealed its importance as an outcome measure in clinical trials investigating fissure sealant efficacy. Of the 32 prospective controlled clinical trials identified over the last 5-year period, 16 reported their results in terms of only retention and not dental caries outcome, 14 reported using retention and dental caries outcome, and two trials reported their results using dental caries but not retention as the measured outcome. This suggests that the number of listed fissure sealant trial reports that included retention but not dental caries as an outcome was eight times higher than the number of trial reports that included dental caries but not sealant retention. Furthermore, only 50% of all trial reports did include dental caries as an outcome compared to 94% that reported on retention.

The status of retention as a leading fissure sealant criterion is based on the consensus that sealant effectiveness is dependent on its full retention (6), which is regarded as the provision of an effective barrier to the oral environment that prevents plaque accumulation in dental pits and fissures and seals in cariogenic bacteria that are
then either killed or at least prevented from multiplying (2,7-9). Resin composites are considered as the sealant material with the highest retention and are therefore seen as superior to sealants consisting of using glass-ionomer cements (GIC) (6). However, despite a higher retention rate of resin sealants over GIC sealants, both appear to have similar effects with regard to caries reduction (6,10). In accordance with the differing outcomes in retention and caries reduction between the two sealant types, two opposing hypotheses have commonly been cited in the dental literature: i) any loss of sealant material in pits and fissures will cause dental caries formation underneath the remaining sealant (7,11), and ii) if the sealant material is only partially lost from pits and fissures, the remaining material continues to prevent caries (11,12). Based on the latter reason, it has been argued that dental caries rate should be considered as the main outcome measure for sealant success instead of retention rate (13). Hence, this leads to two main questions: i) on what logical framework is the consensus for accepting retention as a proxy outcome for caries prevention based, and ii) is such a logical framework valid?

In order to answer these questions, the aim of this study was to establish the underlying logic and critically assess its validity in line with the rules and laws of formal logic and current empirical evidence. In order to achieve this, the objectives of this study were: i) to establish the logical framework of the proposition that full sealant retention is a proxy outcome for caries prevention; ii) to establish a model of dental caries development and the effect of fissure sealants within such a model; iii) to investigate the logical framework in line with the dental caries development model, the rules and laws of formal logic, and the current empirical evidence.

Materials and Methods
A unique deductive logico-empirical approach that consists of a logical investigation of the validity of the proposition’s premise-to-conclusion relationship aided by an empirical investigation of the validity of the proposition’s premise was adopted.

Logical framework for proposition
In order to establish the logical framework of the proposition that sealant retention is a proxy outcome for caries prevention, the following rules of propositional and predicate logic were applied: Hypothetical syllogism (HS), Modus tollens (MT), and Universal quantifier introduction (∀I). Propositional logic is a formal system of logic that studies the connections between different kinds of statements (or propositions) (Kaye SM. Critical thinking: a Beginner’s guide. Oneworld Publications, 2012), while predicate logic is a formal system that studies the connections within a single proposition (Boutelle T, Gibilisco S. Logic demystified. McGraw-Hill Books, 2011). During the application of the rules and laws of propositional/predicate logic in this investigation, the following common logical symbols were used: (\( \wedge \)) = and; (\( \vee \)) = or; (\( \neg \)) = negation; (\( \rightarrow \)) = “If…then…”.

Hypothetical syllogism (HS)
Hypothetical syllogism is a rule of inference in propositional logic where whole statements form propositions that are interlinked as a sequence towards a given conclusion. For example: Proposition 1: if X is the case then Y is the case, Proposition 2: if Y is the case then Z is the case, Proposition 3: If Z is the case then A is the case, Conclusion: therefore, if X is the case then A is the case.

Modus tollens (MT)
Modus tollens is a rule of inference in propositional logic where the consequent (Q) of an initial proposition is denied, thus leading to the conclusion that the antecedent (P) is not true. For example: Proposition: if P is true then Q is true, Denial of the consequent: Q is not true (also expressed as \( \neg Q \)), Conclusion: therefore P is not true (also expressed as \( \neg P \)).

Universal quantifier introduction (∀I)
A Universal quantifier is an indicator in predicate logic that identifies a proposition or statement as always being true. For example: For all cases (x), provided (D) is given, then (M) is true (e.g.,: “All sealed teeth (x), provided the full sealant is retained (Dx), will remain free from dental carious lesions (Mx)”); expressed in logical operators: (∀x) Dx→Mx.

Dental caries model
In order to establish a working model of dental caries development, the elements of the dental caries mechanism, as published by Featherstone (2004) (14), were transferred to a Directed acyclic graph (DAG). The described dental caries mechanism comprised essentially of the observation that acidogenic oral plaque bacteria ferment carbohydrate from the daily diet into organic acids which diffuse into the tooth enamel and dissolve its mineral crystals, thus leading to loss of calcium and phosphate (Demineralisation) and, potentially, development of a carious lesion (14).

In addition to the caries mechanism, the commonly assumed rationale of fissure sealant effects were integrated into the DAG, as follows: i) barrier function...
between acidogenic oral plaque bacteria and mineral crystals in tooth enamel (15), ii) sealing off oral plaque bacteria from carbohydrates (8), iii) exposure of mineral crystals in the tooth enamel to fluoride released from sealant materials (9).

DAGs are graphical tools for the evaluation of causal effects, and can assist in the identification of multiple confounders within a causal system (16,17). They consist of alphabetic letters that represent each variable which, in turn, are connected by arrow lines. These arrow lines represent direct causal links between the variables to form a web of causation.

**Logical and empirical investigation**

Within the established DAG of the caries mechanism (14) and the rationale for fissure sealant effects (8,9,15), the logical framework of the proposition that sealant retention is a proxy outcome for caries prevention was investigated. For this purpose, the logical rules of Hypothetical syllogism (HS) and Reductio ad absurdum (RAA), as well as the logical Law of double negation (LDN) and the Law of contradiction (LOC) were applied.

**Reductio ad absurdum (RAA)**

Reductio ad absurdum is a rule of inference in propositional logic where an assumption is first considered to be correct, and proceeds to evaluate how such assumption leads to a contradiction. For example: 1. suppose P is true, 2. if P is true then Q is true, 3. but Q is not true (¬Q), 4. therefore P cannot be true (¬P).

**Law of double negation (LDN)**

The law of double negation states that a proposition (P) and its double negation (¬¬P) are equivalent: ¬¬P↔P.

**Law of contradiction (LOC)**

The law of contradiction states that a proposition (P) and its negation (¬P) can never both be true: (¬P∧P) = False.

Since valid proxies for primary clinical outcomes are necessary in order to achieve high accuracy in predicting such primary outcomes (18), clinical data (Additional S2 File) from a previous meta-epidemiological study (19) was further analyzed in order to establish the sensitivity and specificity of loss of full sealant retention in the prediction of dental carious lesion development, as well as the number of false positive and false negative prediction rates.

**Clinical data (empirical evidence)**

A previously published study (18) collected clinical trial data on the retention of resin-based sealants in permanent molar teeth, and the caries outcome of these sealed teeth 24 months after sealant placement. From this data, true positive (TP), false positive (FP), false negative (FN), and true negative (TN) caries predictions based on the absence of full sealant retention were established (Additional S2 File). The appraised clinical trials were identified through a systematic literature search, the details of which have been published elsewhere (19). In this previously published study, the extracted data was utilized to compute only the diagnostic odds ratio (DOR) as a summary measure, and not the sensitivity/specificity and the false positive/false negative prediction rates.

**Sensitivity and specificity**

Within the context of this study, the sensitivity was defined as the proportion of true positive (TP) predictions (i.e., the number of sealed teeth that lost full retention and developed carious lesions) in relation to the total number of sealed teeth that lost full retention (20).

The specificity was defined as the proportion of true negative (TN) predictions (i.e., the number of sealed teeth that exhibited full retention and did not develop carious lesions) in relation to the total number of sealed teeth with full sealant retention (20).

The sensitivity/specificity was computed using MetaDisc 1.4 statistical software (21). A useful predictive power was assumed when both sensitivity and specificity were above the 80% threshold. Additionally, the mean sensitivity/specificity of full retention was computed and statistically compared against that of random values using a two-tailed t-test (Biostat 2009 software). The random values were generated using an online random generator (19).

**False positive and false negative prediction rates**

The false positive and false negative prediction rates are defined as the proportion of false positives (FP) and false negatives (FN) in the total number of predictions, respectively. It has been argued that the number of all false predictions (FP+FN) of any predictor should not exceed between 2.5 and 10% of all predictions in order to be considered as valid and, thus, clinically useful (18).

**Results**

**Logical framework for proposition**

Based on the rules of propositional and predicate logic, a logical framework for the proposition that sealant retention is a proxy outcome for caries prevention was developed (Table 1). The framework consisted of 13 separate logical steps, including nine assumptions, two hypothetical syllogisms (HS), one application of the
The framework starts with the two pre-assumptions that, i) if a fissure sealant (FS) is placed then the sealant material (M) has a caries-preventive effect (Assumption A1), and ii) that such effect is based on its full (complete) retention (R) (Assumption A2). Based on both pre-assumptions, which are in line with common consensus (9), it follows that full retention prevents bacterial organic acids from affecting the mineral crystals of enamel (AC) and the fermentable carbohydrates from reaching cariogenic bacteria (CH) (Assumption A3). In such a case, mineral loss is prevented (CP↑) (Assumption A4) along with subsequent dental carious lesion formation (¬C) (Assumption A5). In line with the rule of hypothetical syllogism, it can thus be inferred that full sealant retention prevents carious lesions (R→¬C).

If the inference (R→¬C) is correct and carious lesions (C) are observed (Assumption A6) then, in line with the rule of Modus tollens (MT), there could not have been full sealant retention (¬R). Loss of full sealant retention would lead to bacterial organic acids affecting the mineral crystals of enamel, and the fermentable carbohydrates would be able to reach acidogenic oral plaque bacteria (for fermentation to bacterial organic acids). (Assumption A7). This would lead to mineral loss (Assumption A8) and subsequent formation of dental carious lesions (Assumption A9). In line with the rule of hypothetical syllogism, it can thus be inferred that lack of full sealant retention leads to dental carious lesion development (¬R→C).

Both inferences ([R→¬C] and [¬R→C]) can be combined and, in line with consensus, assumed to be always the case (∀I). Such a generalization may be logically expressed as follows: “For all materials (∀x)M, if used as fissure sealants (x) their full retention prevents dental carious lesions (R→¬C)x and (x) lack of full retention leads to dental carious lesions (¬R→C)x.” This logical proposition can be formally presented using the

<table>
<thead>
<tr>
<th>Line no.</th>
<th>Proposition in plain text</th>
<th>in logical operators</th>
<th>Reference to Line no.</th>
<th>Logical rule</th>
<th>Assumption no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>If a sealant is placed then the material has a caries preventive effect.</td>
<td>FS→M</td>
<td>A1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>If the material has a caries preventive effect then it is completely retained.</td>
<td>M→R</td>
<td>A2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>If the material is completely retained then no bacterial organic acids can affect the mineral crystals of the tooth enamel and no fermentable carbohydrates from the diet can reach acidogenic oral plaque bacteria (for fermentation to bacterial organic acids).</td>
<td>R→¬(AC∧CH)</td>
<td>A3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>If no bacterial organic acids can affect the mineral crystals of the tooth enamel and no fermentable carbohydrates from the diet can reach cariogenic bacteria, then no calcium and phosphate is lost from the mineral crystals of the tooth enamel.</td>
<td>¬(AC∧CH)→CP↑</td>
<td>A4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>If no calcium and phosphate is lost from the mineral crystals of the tooth enamel then there are no carious lesions.</td>
<td>CP↑→¬C</td>
<td>A5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Therefore, if there is complete material retention then no dental carious lesions develop.</td>
<td>R→¬C</td>
<td>3,4,5 HS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Dental carious lesions develop.</td>
<td>C</td>
<td>A6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Therefore complete material retention was lacking.</td>
<td>¬R</td>
<td>6,7 MT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>If there is lack of complete material retention then bacterial organic acids can affect the mineral crystals of the tooth enamel and fermentable carbohydrates from the diet can reach acidogenic oral plaque bacteria.</td>
<td>¬R→(AC∧CH)</td>
<td>A7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>If bacterial organic acids can affect the mineral crystals of the tooth enamel and fermentable carbohydrates from the diet can reach acidogenic oral plaque bacteria then calcium and phosphate is lost from the mineral crystals of the tooth enamel.</td>
<td>(AC∧CH)→CP↓</td>
<td>A8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>If calcium and phosphate is lost from the mineral crystals of the tooth enamel then carious lesions develop.</td>
<td>CP↓→¬C</td>
<td>A9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Therefore, if there is lack of complete material retention then dental carious lesions develop.</td>
<td>¬R→C</td>
<td>8,9,10,11 HS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>If all materials used for placement of fissure sealants are completely retained then no dental carious lesions develop, and if there is lack of complete material retention then dental carious lesions develop (i.e., retention is a proxy outcome for caries prevention).</td>
<td>(∀x)Mx→(R→¬C)x∧(¬R→C)x</td>
<td>6,12 ∀I</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

∀I = Universal introduction.
logical operators: \((\forall x)(Mx \rightarrow (R \rightarrow \neg C)x) \land (\neg R \rightarrow C)x\), and its consequence can be summarized in plain English as “Retention is a proxy outcome for caries prevention”.

**Dental caries model**

In line with published rules for DAG construction (16,17) and elements of the dental caries mechanism [Featherstone (2004) (14)], a Directed acyclic graph was developed and has been presented in Fig. 1.

The graph shows that acidogenic oral plaque bacteria (B) produce organic acids (AC) from fermentable carbohydrates (CH) present in the daily diet (D). These bacterial organic acids (AC) along with the presence of topical fluorides (F) affect the mineral crystals (MC) in the tooth enamel (E). However, the enamel can also be affected by salivary factors (S) such as pH and salivary flow rate, as well as by the patient’s oral hygiene (OH). These influences may cause the mineral crystals (MC) to either lose or gain calcium and phosphate (CP). Loss of calcium and phosphate (CP↓) may be caused by lack of topical fluoride (F) together with high bacterial organic acid (AC) exposure, subsequently leading to formation of dental carious lesion (C), while a gain in calcium and phosphate (CP↑) may be caused by an absence of high bacterial organic acid (AC) exposure and the presence of topical fluorides (F).

When a fissure sealant (FS) is placed, the sealant material (M) obturates the dental pits and fissures (9). This obturation may be complete for all pits and fissures (R) or incomplete (¬R). Any incomplete obturation (¬R) may manifest as either complete (NR) or partial material loss (PR). Equal to full retention (R), partial material loss (PR) may still act as a barrier between acidogenic oral plaque bacteria and mineral crystals in the tooth enamel (15), and the oral plaque bacteria may remain sealed off from carbohydrates (pAC), and the oral plaque bacteria may remain sealed off from carbohydrates (pCH) and continue to release fluoride (F) (Assumption A1). When acting together, all three functions may prevent calcium and phosphate loss (CP↑) which, in turn, may prevent formation of dental carious lesions (Assumption A3). It can thus be inferred that lack of fully retained sealant material may prevent dental carious lesions (Hypothetical syllogism: ¬R→¬C). However, this is contradictory. If it is assumed that the material is not fully retained (Assumption A4), then it should follow that dental carious lesions develop (Assumption A5). If no dental carious lesions develop then, in line with the logic of the proposition that “retention is a proxy outcome for caries prevention,” there should be no loss of complete sealant retention (¬¬R) (Reductio ad absurdum). In line with the law of double negation (LDN), “no loss of complete retention” (¬¬R) is equivalent to “complete retention” (R).

From the logical steps above, it follows that if there is loss of complete retention (¬R), then dental carious...

The alternative logical framework starts with the two DAG-based observations that i) sealant materials (M) may have a caries preventive effect if they are either completely (R) or incompletely (¬R) retained in pits and fissures (DAG observation 1), and (ii) if the material (M) is not completely retained (¬R), then it can either be completely (NR) or only partially lost (PR) (DAG observation 2). While a completely lost sealant (NR) may have no caries preventive effect, a partially lost sealant (PR) may still act as a barrier between acidogenic oral plaque bacteria and mineral crystals in the tooth enamel (pAC), and the oral plaque bacteria may remain sealed off from carbohydrates (pCH) and continue to release fluoride (F) (Assumption A1). When acting together, all three functions may prevent calcium and phosphate loss (CP↑) (Assumption A 2) which, in turn, may prevent formation of dental carious lesions (Assumption A3). It can thus be inferred that lack of fully retained sealant material may prevent dental carious lesions (Hypothetical syllogism: ¬R→¬C). However, this is contradictory. If it is assumed that the material is not fully retained (Assumption A4), then it should follow that dental carious lesions develop (Assumption A5). If no dental carious lesions develop then, in line with the logic of the proposition that “retention is a proxy outcome for caries prevention,” there should be no loss of complete sealant retention (¬¬R) (Reductio ad absurdum). In line with the law of double negation (LDN), “no loss of complete retention” (¬¬R) is equivalent to “complete retention” (R).

From the logical steps above, it follows that if there is loss of complete retention (¬R), then dental carious...
lesions develop and do not develop \((\neg R \rightarrow C) \land \neg (\neg R \rightarrow C)\). Both statements cannot be true as this would violate the law of contradiction, \((P \land \neg P) = \text{False}\). It also negates the universal validity of the claim, \((\forall x)Mx\) that lack of complete retention always leads to dental carious lesion development.

**Empirical investigation**

A total of 90 datasets (DS) from 48 clinical trial reports (Additional S2 File) were identified through the systematic literature search. The details of the literature search have been reported elsewhere (19). From a total of 18,448 predictions, the number of true positive (TP) and true negative (TN) predictions in the test group (prediction by full sealant retention) were 2,350 and 7,536, respectively, and the number of false negative (FN) and false positive (FP) predictions were 5,481 and 5,977, respectively.

The computed results indicate a mean sensitivity (SD) of incomplete sealant retention of 37.9% (standard deviation [SD] = 27.8%) and a mean specificity of sealant retention of 67.6% (SD = 28.4%). When the values were compared against random values of 30.5% (SD = 25.7%) and 58.7% (SD = 31.6%), respectively, a non-significant sensitivity \((P = 0.06)\) and a borderline specificity \((P = 0.04)\) was observed.

The overall false prediction rate was 33.7%, with 16.9% and 16.8%, false negative and false positive predictions, respectively.

**Discussion**

The aim of this study was to establish the underlying logic of the proposition that fissure sealant retention is a
proxy outcome for dental caries prevention, and to critically assess its validity in line with the rules and laws of propositional and predicate logic and current empirical evidence.

Study limitations
This study considered the investigated proposition under the rigid rules and laws of formal logic which, in its strict format, is seldom applied in everyday life. It could be argued that in line with common sense, a high sealant retention rate will always act as a beneficial factor in the prevention of dental carious lesions and thus should be permissible as being synonymous with caries prevention. Such a synonym would imply an equivalence of retention with caries prevention, but only in a less strict, semantic sense.

It may further be regarded as common-sense that dental carious lesion development can follow many pathways (18,22), including genetically based enamel insufficiencies, very high frequent-sugar intake, and lack of any effective oral hygiene (all in cases where sealants are in place but alone prove too weak to withstand the stronger cariogenic effect of such factors). Thus, fissure sealants may only provide protection in some instances and only if their retention is high enough or complete. This would mean that full sealant retention is a necessary but not a sufficient factor (when considered alone) for caries prevention. In line with such argumentation, it would follow that it is important to know which material can fulfill complete retention best, making it important to investigate sealant retention rates in clinical trials instead of the caries prevention rate as other cariogenic factors would act as confounders of the true sealant material effect. For these reasons, the application of rigid logical rules and laws to the proposition that retention is a proxy outcome of caries prevention may be considered as misguided.

However, such argumentation accepts that retention cannot be a proxy outcome for dental caries due to multiple confounding factors. It further does not clarify to what extent full retention actually prevents carious lesions, and at what threshold partial retention ceases to be caries preventive. Another consideration is that dental patients may not really worry about how long fissure sealants are retained, but rather how long carious lesions in their teeth remain prevented (23). In this regard, oral care providers have an ethical duty to patients to offer only such interventions that have been shown to be effective in achieving their primary, patient-centered clinical outcomes, like the prevention of carious lesions (General Medical Council UK. Good medical practice. Manchester, 2013; Medical Board of Australia. Good medical practice: a code of conduct for doctors in Australia. Canberra, 2014). For that reason, fissure sealant materials should be investigated to identify which material may achieve these primary outcomes best. Any confounding effects can be controlled by use of randomization in clinical trials (24).

Further limitations of this study may include those posed by the included data (Additional S2 File), which have been discussed elsewhere (19). However, the data has been found to be in line with other published reports in terms of its internal validity (25). Another limitation may be the omission of considering the caries development process in line with the re-mineralization/de-mineralization dynamic as presented by Featherstone (14). This dynamic was discussed in terms of a caries balance that includes a balance between pathological and protective factors. Only if the former supersedes the latter does dental carious lesions occur. However, for the sake of simplicity, it was assumed in this study that pathological factors such as acidogenic bacteria, frequency of fermentable carbohydrate ingestion, and reduced salivary function were stronger than the protective factors (saliva flow and components, proteins, antibacterials, minerals, protective dietary components), as listed by Featherstone (14), thus leading to dental carious lesions. Within the context of this study, this omission will not have affected the logical framework of the investigated proposition that retention is a proxy outcome for caries prevention.

Study results
The logical framework of the investigated proposition has been shown in Table 1. Using the DAG (Fig. 1), two flaws in this framework were identified: i) lack of complete/full retention (¬R) may indeed mean complete loss of retention (NR) and therefore complete loss of the preventive sealant effect, but can also mean partial retention (PR), and ii) such partial retention (PR) may sufficiently prevent loss of mineral crystals (CP↑) and consequently prevent carious lesions (¬C) (Table 2). Both are a result of the logical contradiction that if there is lack of complete/full retention (¬R) then carious lesions develop (C) and no carious lesions develop (¬C): (¬R→C)∧¬(¬R→C). According to the logical law of contradiction, both cannot be true at the same time (Reductio ad absurdum).

It may be argued that in clinical practice (= the “real world”) both (¬R→C) and (¬R→C) may very well be true at some point in time, and that the logical application of the rule of contradiction is too rigid. However, such an argument would also mean that complete retention couldn’t be a proxy outcome for caries prevention.
because in such a case a direct association between full sealant retention and caries prevention is missing. A less strict argument could be made that \((R \rightarrow \neg C)\) the first part of the established logical proposition (Table 1) does not always have to be the case but only most of the time and beyond the play of chance, in order to be clinically meaningful. The current empirical evidence from clinical trials (19) presented in Table 3 does not support such a claim. If complete retention \((R)\) was a true proxy outcome for caries prevention \((C)\) then the latter would correctly predict the absence of carious lesions with sufficiently high accuracy. Despite being (borderline) statistically significantly higher than random values \((P = 0.04)\), the specificity established in this study lies below the 80\% threshold for clinical relevance (67.6\%, SD = 28.4\%). In addition, the rate of false negative (FN) prediction was found to be 16.9\%, which is above the acceptable limit for total prediction errors (2.5-10\%) (18).

The second part of the established logical proposition that lack of complete retention leads to dental carious lesions \((\neg R \rightarrow C)\) claims that \((\neg R)\) can correctly predict the occurrence of dental carious lesions. The current empirical evidence from clinical trials (21) does not support such a claim either. Firstly, the sensitivity also lies below the 80\%-threshold (37.9\%, SD = 27.8\%); secondly, the sensitivity of \((\neg R)\) does not significantly differ from that of random values \((P = 0.06)\); and thirdly, the rate of false positive (FP) prediction was also above the acceptable limit for total prediction errors (16.8\%).

Table 3 Summary of empirical and logical evidence

<table>
<thead>
<tr>
<th>Full proposition</th>
<th>Proposition parts in plain text</th>
<th>Proposition parts in logic operators</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Retention is a proxy for caries prevention” (Table 1)</td>
<td>((\forall x)) (Mx \rightarrow (R \rightarrow \neg C)_x \land (\neg R \rightarrow C)_x)</td>
<td>((\forall x)) (Mx) (\rightarrow \neg C) (\land \neg R \rightarrow C)</td>
<td>Results</td>
</tr>
<tr>
<td>If there is complete material retention then no dental carious lesions develop.</td>
<td>R (\rightarrow \neg C) Results</td>
<td>Evidence in support of proposition</td>
<td>Evidence in support of proposition</td>
</tr>
<tr>
<td>If there is lack of complete material retention then dental carious lesions develop.</td>
<td>(\neg R \rightarrow C) Results</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

FP = False positive; FN = False negative; CI = Confidence interval; DOR = Diagnostic odds ratio.

The third part of the proposition consists of the universality claim \((\forall x)\) that lack of complete retention always leads to dental carious lesions development. Universal claims or statements are falsifiable by single observations to the contrary (Popper K. The logic of scientific discovery, Hutchinson, 1980). The multiple false positive and false negative results (Table 3) show that the universality claim cannot be true.

In summary, all three parts of the proposition that retention is a proxy outcome for caries prevention are invalidated by logical and empirical reasons (Table 3). Furthermore, the empirical evidence (Additional S2 File) utilized in this study focused only on the predictive accuracy that a proxy needs to have in order to predict its primary outcome. More stringent standards such as the Prentice criterion (26) exist for surrogate outcomes in relation to their primary endpoints. A published systematic review (27) investigated the validity of sealant retention in line with the Prentice criterion and was unable to conclude validity. The Prentice criterion states that in order for a surrogate endpoint to be considered valid: i) the surrogate needs to correlate with its true clinical endpoint, and ii) the surrogate/clinical endpoint correlation needs to be independent from the treatment type applied (26). Sealant retention could not be considered a valid surrogate for caries because it did not exhibit a robust correlation with its primary endpoint, nor was it independent from the type of sealant material placed
(26).

Against the background of lack of predictive power (19), lack of robust correlation with its primary endpoint (27), lack of independence from the sealant material used (27), as well as the lack of a robust logical rationale as established in this study, it is difficult to understand why sealant retention should be regarded as the single most important outcome measure for fissure sealant efficacy or why a consensus persists with regard to consideration of sealant retention as a proxy outcome for caries prevention? Instead, the adoption of the caries reduction/prevention rate as a standard measure for fissure sealant success appears to be clinically more relevant.

In conclusion, the logic behind the proposition that retention is a proxy outcome for caries prevention may appear sound and based on common sense. However, the logic of this proposition is in fact flawed and contradicted by the current empirical evidence gathered from controlled clinical trials and, thus, cannot be considered to be valid.

Conflict of interest
Non declared.

References
Supplementary Files
Additional S1 File: Literature search
Additional S2 File: Empirical evidence
Please find supplementary files; doi: 10.2334/josnusd.16-0497