Secondary caries: What is it, and how it be controlled, detected and managed?

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Short title: Detecting and managing secondary caries

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Abstract

Objectives: To define secondary caries, assess how to control, detect and treat it. This review serves to inform a joint ORCA/EFCD consensus process.

Methods: Systematic and non-systematic reviews were performed or consulted. Where applicable, Bayesian network meta-analysis was used to synthesize data. Risk of bias of included studies was assessed via the Cochrane Risk of Bias tool, or risk of bias had been assessed by included reviews themselves.

Results: Secondary caries is characterized by the presence of a wall (interfacial) lesion, distinguishing it from caries adjacent to restorations, which are not necessarily associated with a restoration. For comparing different contemporary adhesive strategies and restorative materials, a systematic review of randomized trials (published 2005-2017) was performed. 51 studies (performed in controlled settings, largely small cohorts and over short or medium follow-up periods) were included, often yielding no secondary caries lesions at all regardless of the group. Network meta-analysis found great uncertainty. With some chance, 3-step etch-and-rinse and 1-step self-etch instead of 2-step etch-and-rinse- or self-etch adhesives lower the risk of secondary caries development. For restorative strategies, resin-modified glass ionomer yielded high chances of preventing secondary caries development, while the differences between various resin composites or conventional glass-ionomer cements were limited. Current detection methods for secondary caries are only sparsely validated and likely to be prone to over-detection. Using specific methods or combining them was suggested. Detected secondary caries can be approached using the “5R” protocols, which may increase the longevity of the restoration, but are limited by indication.

Conclusions: There is sparse data towards the nature of secondary caries and how to control, detect and treat it.

Clinical significance: Despite often claimed to be a major complication of restorations, there is surprisingly little data on secondary caries from clinical studies. Longer-term studies may be needed to identify differences in secondary caries risk between materials and to identify characteristic features of progressive lesions (in need of treatment).

Introduction

Secondary caries has been defined as “lesions at the margins of existing restorations” [1]. There is debate around the pathogenesis of these lesions. In many circumstances, these lesions may not be “secondary caries” in the sense that they are caused or causally associated with the restoration, but primary carious lesions adjacent to existing restorations. Such caries adjacent to restoration / sealants (CARS) occurs when the caries process has not been sufficiently addressed on a patient level and the surface next to the restoration becomes carious as a result of this ongoing caries activity, without the restoration being causally associated [2-4]. CARS often occurs when surfaces next to restorations become susceptible to ongoing cariogenic attack (e.g. in case of gingiva recession for proximally extended and formerly subgingival restorations). On the other hand, “true” secondary carious lesions (i.e. those causally associated with the restoration) have been found in cases of defective restorations, mainly those with significant margin defects (interfacial gaps, ditches etc.), allowing acidic fluids or biofilm to enter the interface between the restoration and the tooth structure. The result is not only demineralization on the tooth *surface*, as typically occurs in primary carious lesions, but along the *interface*, resulting in the classical morphology of such secondary lesions (Figure 1), with a surface lesion (formed largely independent from the defect, but possibly facilitated by enhanced biofilm formation along the tooth-restoration margin area), and a wall lesion along this interface. Wall lesions are the typical sign of ”true” secondary caries [4-7].

There is some debate around the nature and size of the defect required to allow formation of such wall lesions. A number of in vitro studies, using various secondary caries models, have been performed, yielding threshold gap sizes of the defect between 60 µm and 1000 µm [8, 9]. In-situ studies confirmed the range of these gap sizes. More recent studies found masticatory loading on the restoration to enhance wall lesion formation, enabling such formation also along relatively small gap sizes, possibly as the cyclic loading facilitates fluid (and dysbiotic biofilm) penetration along the interface [10-12]. Findings from in-vivo studies, however, could not necessarily confirm such threshold gaps sizes or effects of loading, mainly due to methodological limitations. However, also in-vivo, wall lesions have not been found without gaps being present [4].

The presence of gaps may be the result of an imperfect initial placement of the restoration, for non-compensated polymerization shrinkage or insufficient light-curing of the material (with a subsequent wash-out of un-cured components) [13]. Long-term, defects and gaps may also form by hydrolytic degradation of the hybrid layer and hence the interface in case of adhesive (resin-based) restorations [14, 15].

Can we control secondary caries risk?

A number of factors have been evaluated for their association with secondary caries risk. If they were to be controlled, the risk for secondary caries could be controlled, too.

The most frequent ones, synthesized in a recent review [16], are:

- Surface location. The vast majority of secondary carious lesions (up to 90%) are found at the gingival margin of restorations, regardless of the restoration material [17, 18]. It was further speculated that “deeper” proximal restorations, i.e. those extending to the cementum-enamel junction or beyond, show higher risks of secondary caries, as the dental substrate is not enamel, but cementum and dentine in this case [19], but also as restoration placement may be more challenging for these deeper restorations (see above). The sparse data available does not necessarily confirm this hypothesis, though [20].
- Patients’ caries risk / susceptibility. The risk of restoration failure due to secondary caries is significantly increased in high-risk caries patients compared to low-risk ones [21, 22]. Most data is collected from posterior restorations; in anterior regions, secondary caries is less likely to occur [23].
- Patients’ age. It remains unclear if age mainly serves as proxy for caries susceptibility (being higher in very young and the older patient), or if there is truly an association between secondary caries susceptibility and age. It is also conceivable that the placement of restorations will come with different challenges in different age groups, which may be reflected in the risk of secondary caries, as discussed.
- Socioeconomic status. While the socio-economic status may, indirectly via behavioral traits, affect caries susceptibility (see above), it remains unclear if it is also associated with “different” restorations (placed differently, using different materials or protocols). There is evidence that socioeconomic status is associated with longevity of restorations and secondary caries [24, 25].
- Operator skill variability. As discussed, secondary caries is partially associated with the quality of the restoration placed. Besides the patient as one main factor, the operator is often seen as the second main factor impacting on restoration longevity and risk of secondary caries (both being possibly more relevant than the specific restorative protocol or material, see below). Operator’s experience and care during placing the restoration will affect its integrity and long-term survival. Practice-based studies demonstrate the impact of operators on restoration longevity [24-27].
- Detection methods and criteria. As discussed below, detecting secondary caries is a challenge. Most detection methods and criteria have limited accuracy [28]. While, of

course, detection methods and criteria will not affect the “development” of secondary caries, they will determine how often an identified entity will be defined as secondary caries or not. Detection methods and criteria will, for example, impact on the reported incidence rates of secondary caries. In this sense, it is unclear at present if the high incidence rates reported from long-term data, mainly stemming from non-controlled cohorts, are fully ascribable to secondary caries. In many instances, discolorations or clinically irrelevant imperfections may have been identified as secondary caries [18, 29, 30]. At present, there is sparse evidence demonstrating what kind of characteristics an identified defect needs to have to progress into a state where care is undoubtedly needed, or to remain in the status quo long-term, possibly never progressing and hence never needing care [31].

The factor which has been evaluated most frequently, though, is the restorative material. A large number of studies comparing different materials have assessed secondary caries, either *in vitro*, *in situ* or clinically. In-situ, a recent systematic review could not identify significant and consistent differences in secondary caries development next to different restorations [32]. The authors of the review included nine studies (132 patients, 8 materials), and performed network meta-analysis for synthesizing the results. They found that any material rankings come with uncertainty and identified ambiguity or even contradiction between studies. Hence, they raised doubts as to the validity and transferability of the existing evidence from such in-situ studies and called against applying the findings from these studies, especially single studies, to derive clinical recommendations, mainly as the findings from these single studies seem to be driven by methodological decisions, not true differences between materials, in many cases. Such heterogeneity applies to in vitro studies [33-35].

To derive clinical recommendations, then, the evidence from clinical studies should be sought. Ideally, randomized clinical trials should be used to answer the question “Which restorative strategies or materials should be employed to reduce the risk of secondary caries?”.

Systematic review on secondary caries and restoration strategies and materials

A systematic review was therefore performed to collect and appraise and synthesize randomized controlled studies on restorative strategies and materials, i.e. adhesive techniques and restoration materials, and their impact on secondary caries.

Inclusion and exclusion criteria

The inclusion criteria used were as follows: (1) prospective clinical trials, (2) studies comparing at least two different restorative adhesive techniques, restorative materials, or their combinations, (3) studies with a follow-up period of at least two years; this was done to increase the chance of secondary caries development in the trials, (4) studies needing restorations for the treatment of primary caries or complete replacement of a defective restoration, or for non-caries cervical lesions (NCCL), (5) for publications reporting on different follow-up phases of a specific trial, only the most recent publication (longest follow-up) was included.

The exclusion criteria were as follows: (1) Retrospective or observational studies. (2) Studies performed on primary teeth. (3) Studies evaluating restoration repairs, not newly placed restorations. (4) Studies evaluating full coverage direct or indirect restorations. (5) Studies tested outdated materials, which are not available currently on the market. To restrict the review to materials available and relevant today, the search period was restricted (from 2005 onwards, see below).

Notably, such a review may not yield a significant number of studies involving one of the most commonly used materials, dental amalgam. However, with the UNEP-led international decision to phase-down and possibly even phase-out dental amalgam in the future, as well as amalgams now being only a relatively small proportion of daily restorative care in many countries, but also accounting for the fact that amalgam has not been compared against most non-amalgam, contemporary materials, it was decided to accept this caveat. It should be highlighted that data comparing amalgam with alternatives, mainly resin composites, has shown amalgam to yield lower risks of secondary caries [36].

Outcome

The outcome for this review was the occurrence of secondary caries assessed via either visual-tactile method or radiographs (i.e. the most widely used detection methods, see below). Secondary caries could have been evaluated explicitly or as part of a criteria set like FDI or United States public health service (USPHS) criteria.

Information sources and search strategy

Clinical studies evaluating different restorative strategies or materials were searched in the database PubMed (search period 2005-2019, search time March 2019). The search terms and strategy are depicted in Figure 2. The reference lists of the included studies were screened to identify possible relevant studies (cross-referencing).

Study selection and data collection

Two independent researchers (HA, FS) performed the electronic research and screened titles and abstracts to decide consideration for full-texts. Data extraction as well as the risk of bias assessment was performed one of the authors (HA) and verified by a second author (FS). Disagreements between the evaluators were resolved through discussion. A spreadsheet was used for data extraction and management.

Data items and categorization

The following data were collected: study, year, participants information (age, gender, sample size), restorative strategy or materials (commercial name and details, see below), restoration (number, number of surfaces, reason for restoration [caries, replacement of defective restoration or non-caries cervical lesions]), follow-up (duration, intervals, method) and number of detected secondary caries lesion in each follow-up interval.

For data analysis, the restorative strategies and materials were categorized as follow:

1. For adhesive strategies, four groups were used: 2-step etch-and-rinse (2-ER), 3-step etch-and-rinse (3-ER), 1-step self-etch (1-SE), 2-step self-etch (2-SE), no adhesive at all.
2. For restorative materials, the following groups were used: Glass-ionomer cement (GIC), resin-modified glass-ionomer cement (RMGIC), compomer (C, polyacrylic acid-modified composite). Resin composite materials were further sub-classified according to the matrix, filler particles and application mode [37]: nanofilled (N), nanohybrid (NH), microfilled (M), microhybrid (MH), bulkfill (BF), silorane-based (Si).

Manufactures and categories of the used adhesive strategies and restorative materials are presented in appendix Tables S1 and S2, respectively.

Confidence in data

Selection bias (random sequence generation, allocation concealment), detection bias (blinding of participants and personnel, blinding of outcome assessment) and reporting bias (selective reporting, incomplete outcome data) were recorded, and assessed according to the Cochrane risk of bias tool for randomized clinical trials [38].

Synthesis

Network meta-analyses (NMA), yielding pairwise, indirect and network estimates, were performed, one on adhesive strategies and one on restorative materials. Studies which had compared combinations of adhesive strategy and restorative material, but did not allow to separate the effects of these two factors, were not entered into NMA. There was no missing data. In case of zero events (no secondary caries lesions) occurring in both groups, a continuity correction of +0.5 was applied.

Pairwise, indirect and network (mixed comparisons) estimates were made using Bayesian random-effects modelling and Markov Chain Monte Carlo (MCMC) simulations using JAGS implemented in the R package *gemtc* 0.8-2 [39]. Networks of interventions were constructed by plotting different treatments (as nodes) and comparisons (as edges) [40, 41]. Normal likelihood was used to model the data [42], using non-informative priors with a normal distribution for the mean, and a uniform prior for the random-effects standard deviation. The parameter range for each network was obtained from data using the *gemtc* package. The first 20,000 MCMC iterations were discarded as “burn-in” and then further 80,000 iterations were undertaken for 4 chains with a thinning of 1. The convergence was assessed based on the Brooks-Gelman-Rubin criteria [43] and inspection of trace plots.

Odds Ratio (OR) and their 95% credible intervals (95% CrI) were reported. Credible intervals are the range of estimated parameters after exclusion of extreme values [44]. Mean ranks and the cumulative ranking curve (SUCRA) [45] were used to rank groups (adhesive strategies, restorative materials). Rankings and SUCRA-values were graphically displayed [46].

Heterogeneity was assessed via a common estimate (total I^2 value) for the heterogeneity variance across different comparisons [47]. Comparison adjusted funnel plot were assessed to check for the existence of publication bias [48].

Results of the search and included studies

From 661 identified studies, 51 were included (Fig. 2). The included studies are described in more detail in appendix Tables S3 (adhesive strategies) and S4 (restorative materials). The excluded studies, with reasons for exclusion, are shown in appendix Table S5.

Nineteen studies assessed secondary caries risk depending on different adhesive strategies, 32 on restorative materials. The studies were published between 2005 and 2017 and included a mean of 40 (range: 8 - 90) participants and 45 (range: 50-200) placed restorations. Mean follow-up was 43 (range: 24-180) months. Generally, secondary carious lesion occurrence was a rare event; the majority of studies did not find any lesions, which may be grounded in the shorter follow-up period. Pooling the available studies revealed two networks, one on adhesive strategies (Fig. 3a) and one on restorative materials (Fig. 3b). The included studies were largely of unclear or high risk of bias (Tables S6, 7). There was no indication for publication bias when inspecting funnel plots (appendix Fig. S1 and S2).

Results of synthesis

For adhesive strategies, most comparisons were made between 1- and 2-step self-etch adhesives or 2-step etch-and-rinse adhesives (Fig. 3a). Pair-wise estimates yielded no significant difference between the four established strategies. When ranking probabilities and the resulting SUCRA-plots were evaluated, there was some probability that 3-step etch-and-rinse adhesives were associated with a lower risk of secondary caries (not one secondary lesion was detected in the studies including that strategy), followed by 1-step self-etch and 2-step etch-and-rinse adhesives. 2-step self-etch adhesives showed the highest risk, while the differences generally were limited (Fig. 4). Overall, these findings are consistent with studies from in-vitro data, with 3-step etch-and-rinse adhesives being considered the gold standard and 2-step self-etch adhesives not performing particularly convincingly. Again, it is highlighted that these findings are based on only few events; overall, all adhesives seem to be able to prevent secondary caries development, at least over the limited follow-up period found in the considered RCTs.

For resin composites, a less densely populated network with more groups emerged, with some comparators (namely GICs) being only loosely connected. The most frequently considered materials were microhybrid, nanofilled or nanohybrid resin composites (Fig. 4b). Again, only few secondary carious lesions developed in the included trials. Pairwise estimates yielded by network meta-analysis found no significant differences between most material comparisons, with the notable exception of resin-modified glass-ionomer cements (RMGICs), which were significantly superior to most alternatives. This was also reflected in ranking probabilities and SUCRA-values (Fig. 5), where RMGICs were ranked highest, followed by polyacrylic acid-modified composites (compomers) and nanohybrid resin composites. Nanofilled, microhybrid, microfilled and bulkfill resin composites performed similarly, with mediocre probabilities of not developing secondary carious lesions. Silorane-based materials and GICs showed the lowest ranks and SUCRA-values, indicating some increase likelihood of secondary caries development according to the included trials. Overall, however, the data supporting this analysis were sparse; findings may change as new data emerges. Overall, it can be concluded that RMGICs may have some potential to prevent secondary caries development, but that also for other materials, only a limited number of lesions occurred within the follow-up of the included trials.

Findings and limitations

It is highlighted that the chosen classification of materials is only one of many possible. A recent study found that for most materials, similar conclusions will emerge regardless which classification is employed in a meta-analysis [37]. It is also emphasized that particular properties of restorative materials, e.g. buffering capacity, have not been addressed in this review, but have been found potentially relevant for secondary caries development [49]. Lastly, it is clear that over the follow-up period of the included RCTs, most of which were performed in low-risk patients under controlled (university) settings, only a few lesions developed. Longer-term, practice-based studies found higher incidence in secondary caries [50, 51].

Overall, however, the impact of the adhesive strategy or restorative material on secondary caries risk seems to be limited, Moreover, technical factors including enamel beveling or the use of rubber dam isolation during the placement of resin composites have been assessed for their relevance on restoration failure (not only secondary caries), but have not been shown to be related to secondary caries risk or, generally longevity [52].

In conclusion, patient- and operator-level factors seem to be decisive for controlling secondary carious lesions. The risk for such lesions may be moderated, but not generally guided by the adhesive protocol used, restorative material or restorative steps, as long as established materials are used explicitly according to manufacturers' instructions. Severe flaws during placement of restorations will, however, come with the short- or long-term risk of defects, like interfacial gaps, which will facilitate secondary carious lesion induction.

Detecting secondary carious lesions

As discussed, there is currently only limited evidence on how to control secondary carious lesion development. Early detection of secondary lesions may allow provision of less invasive treatment options like surface refurbishment, re-sealing or repair instead of complete removal and replacement of restorations (see below). Currently, there is no standard for the detection of secondary lesions and dentists seem to rely mainly on visual, probing (tactile assessment) and radiographs [53].

Detection of secondary lesions can either be highly sensitive, detecting nearly all lesions, but coming with a concomitant high risk of false positive diagnoses, or highly specific, avoiding such false positive diagnoses but consequentially missing many lesions. There will always be, to some degree, a trade-off between sensitivity and specificity and the resulting over- and under-detection or -treatment [28].

A variety of methods are available to detect secondary lesions, including visual, tactile, radiographic, laser fluorescence and quantitative light-induced fluorescence assessments. A recent review [28] summarized the available evidence on these detection methods and their accuracy. For this review, clinical or in vitro studies investigating the accuracy of these five detection methods on natural or artificially-induced secondary lesions were included. A diagnostic accuracy meta-analysis was performed and sensitivity, specificity, positive and negative likelihood ratios were estimated. From 1179 screened studies, 23 were included; all but two were performed *in vitro*, all included permanent posterior teeth and all had high risk of bias. Lesions were mainly assessed in permanent teeth (n=21); two studies assessed primary teeth. Lesions were adjacent to amalgam (n=13), resin composites or other tooth-colored materials (n=7); three studies assessed both materials. Visual detection included the assessment of discoloration (n=6), staining (n=3) or other visually detectable changes (n=3). Tactile detection included the assessment of ditching (n=8). Radiographic detection (n=12) and combined visual-radiographic assessment (n=1); laser fluorescence (n=8); and quantitative light-induced fluorescence (n=3) were also investigated. Visual (n=11 studies), radiographic (n=13) and laser fluorescence detection (n=8) had similar sensitivities (0.50 to 0.59) and specificities (0.78 to 0.83). Tactile assessment (n=7) had low accuracy. Light-induced fluorescence (n=3) was sensitive, but showed low specificity. Recent in-vitro data found near-infra-red light transillumination potentially useful to detect secondary lesions, with similar accuracy as radiographic assessment and being superior to visual-tactile detection [54].

In summary, visual, radiographic and laser-fluorescence detection are potentially useful to detect secondary lesions. Near-infrared transillumination may also be useful, but data at the present time, is still scarce. For tactile and quantitative light-induced fluorescence assessment, the data are both sparse and not currently promising.

Given that secondary lesion detection is performed as part of a routine screening appointment and possibly applied repeatedly, there is some data indicating that specific measures should be prioritized, as secondary lesions progress only slowly and missed lesions may be detected at the next screening round, or to combine sensitive and specific methods [31]. Avoiding false-positive diagnoses, which lead to costly and invasive overtreatment, seems highly relevant, but may not be current standard in practice.

Dealing with secondary caries: Repair or replace restorations?

If secondary caries is detected, dentists are faced with a number of treatment options. Conventionally, such defective restorations were completely removed and replaced. The repeated complete replacement of defective restorations results in excessive removal of dental hard tissue and shortens the lifespan of the tooth [55-57]. This is the reason why partial correction, using repair, re-resealing or refurbishing partially defective restorations [58] has become popular [59-61]. Such partial corrections are accepted among dentists [59], and a wide range of protocols of how to correct (mainly repair) such restorations exist (see below).

Repairing restorations is not only considered to preserve tooth structure and reduce the risk of treatment-related complications, but also can be less time-consuming and less costly compared to the complete replacement of partially-defective restorations. On the other hand, the survival probability of repair restorations might be inferior to that of replaced restorations [62, 63]. Data from a range of studies [21, 51, 64-66] indicate that annual failure rates (AFR) of newly placed or completely replaced restorations was in the range of 1.1%-2.2% for resin composite and 2.1-3.0% for amalgams, when larger load-bearing restorations (i.e. those where secondary caries as well as the decision between complete and partial replacement is most relevant) are considered.

The recent Cochrane review on this topic repair vs. replacement did not include any studies, which is not helpful [67]. However, a recent systematic review and health economic analysis assessed the risks of complications after repairs compared with new or completely replaced restorations of larger cavities [68]. Five studies, all but one not being randomized controlled trials but non-randomized studies, were included. In a rather simple synthesis, the relative risk of complications in repaired versus new/replaced restorations was estimated as sample-size weighted means and ranges of AFR (Table 1).

Based on this sample and extrapolating to larger restorations, regardless of the failure type of the first restoration (fracture, secondary caries), long-term data indicated a possible, but not consistently increased risk of failure in repaired versus newly placed or completely replaced restorations. More importantly, however, is the question if such a small increase is acceptable given that the original restoration did not need complete removal and replacement in the first place. Acceptability has been assessed by the same study from a cost-effectiveness perspective [68]. The study used a modelling methodology to follow repaired or replaced restorations over a lifetime and hence considered the possible detrimental effect of not repairing, but fully removing the old restoration, on tooth longevity.

For partially defective resin composite restorations, the study found repair minimally costlier than replacement, but also minimally more effective. For amalgam, repair was much costlier (mainly as complete replacement of amalgam was rather inexpensive) and minimally more effective. The larger (extended) the partially failed restoration, the more cost-effective was the repair, especially for resin composite. Notably, the study assessed if repair was a good option in case the original complication was secondary caries, which is of relevance for the present review. In this case, repair was highly cost-effective (the opposite was the case if fracture was the reason of initial failure). The authors ascribed this to the fact that in restorations failing due to fracture, high physical stress may the reason and repairs may not be sufficiently suited to withstand this. In contrast, in case of secondary caries and as discussed, secondary caries risk is mainly affected by the patient/operator, not a material or technique dependent variable. It may not matter too much if the restoration is replaced or repaired (as long as the margin integrity is provided). If accessible, repairing (or refurbishing, resealing) restorations partially defect due to secondary caries seems advisable.

Establishing a sustainable bond to different restorative substrates can be challenging and requires adhesive protocols tailored to the specific materials to repair. A number of repair protocols are available in order to guide clinicians in treatment steps necessary for establishing a sustainable bond to defective restorations. In general, basic requirements for establishing an adhesive bond do not differ between dental hard tissues and restorative substrates. These requirements comprise creation of a micro-retentive and wettable surface on the substrate to bond to and application of bonding agents in order to create micro-mechanical and chemical adhesion. Based on available repair protocols the following recommendations for placement of repair restorations can be made [69, 70]:

- Defective parts of the restoration should be removed and the restoration surface of the cavity roughened by use of diamond burs.
- Depending on the type of restorative material to repair, different surface pre-treatments can be recommended:
    - Resin composite and amalgam surfaces should be air abraded with Al_2O_3.
    - Silicate ceramic surfaces can also be air abraded with Al_2O_3. Alternatively, acid etching using hydrofluoric acid can be performed if contamination of gingiva, enamel and dentine can be avoided.
    - Metallic and oxide ceramic surfaces should be air abraded using either Al_2O_3 or silica coated Al_2O_3. The latter one is used to create a silicate layer on the restoration surface by tribo-chemical coating. However, caution is required when dentine surfaces are also involved as contact with the silica coating can hamper adhesion of self-etching bonding agents to the dentine surface [71].
- Areas of dental hard tissue in the cavity to be repaired should be etched with phosphoric acid. Phosphoric acid etchant can also be applied on composite or glass based ceramic surfaces to obtain a cleaning effect. However, contact of phosphoric acid to metallic surfaces and zirconia should be avoided as this might hamper the adhesion of 10-methacryloyloxydecyl-dihydrogen-phosphate (MDP) containing primers [72].
- Depending on the chemical composition of the restoration surface, different primers can be used to create chemical adhesion:

    - Application of a silane coupling agent can be recommended for surfaces containing silicates. This is the case for silicate ceramics, composites and silica-coated metallic or oxide ceramic surfaces.
    - Metal or zirconia-primer should be used for pre-treatment of metallic or zirconia surfaces if no silica coating has been performed.
    - Alternatively, universal primers containing components (e.g. silanes, MDP, sulfur-containing monomers) for chemical bonding to a variety of surfaces can be used.
- Application of a dental adhesive system and placement of the resin composite repair restoration should be performed as usual.

Overall, repairing partially defective restorations seems to have advantages for the longevity of the initial restoration, may slow down the restorative spiral of ever escalating hard-tissue loss, and hence provide longer retention times for teeth. In case secondary caries was the reason for repairs, these may come with a high cost-effectiveness. However, performing repairs is challenging and requires a number of steps, which may be compromised given their high technical requirements. Moreover, only in certain indications (area to be repaired accessible, remaining restoration intact, patients accepts repair, repair steps can be performed as described), repairs should be attempted.

Conclusions

Secondary carious lesions may be CARS, without any causal association with the adjacent restoration, or “true” secondary lesions, which are characterized by the presence of an interfacial “wall” lesion. Such true secondary lesions only develop in case a sufficiently large interfacial gap is present. Main drivers of both CARS and “true” secondary lesions development are the patient and operator factors. There is limited indication for significant differences in secondary caries risk adjacent to different contemporary restorative materials. It is also not clear if different adhesive strategies have a clinically relevant impact on secondary caries risk. Established standard materials or strategies seem to yield only low secondary caries incidence in controlled studies over short- and mid-term perspective. The high incidence rates found in less controlled long-term studies may be ascribed to the fact that secondary caries occurs rather late in the lifespan of a restoration, but may be aggravated by current detection methods not being sufficiently accurate to detect secondary lesions, with over-detection being a frequent problem for many rather sensitive detection methods. If secondary lesions are found while the restoration is intact in most other parts, dentists may aim to retain these parts and repair the defective areas. In other circumstances, such repairs may not be an option; depending on the defect, of its accessibility, the general status of the restoration or patients’ wishes.

Compliance with Ethical Standards

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References

[1] I.A. Mjor, F. Toffenetti, Secondary caries: a literature review with case reports, Quintessence international (Berlin, Germany : 1985) 31(3) (2000) 165-79.

[2] E.A. Kidd, Diagnosis of secondary caries, Journal of dental education 65(10) (2001) 997-1000.

[3] F. Schwendicke, M. Kern, U. Blunck, C. Dorfer, J. Drenck, S. Paris, Marginal integrity and secondary caries of selectively excavated teeth in vitro, Journal of dentistry 42(10) (2014) 1261-8.

[4] J.L. Ferracane, Models of Caries Formation around Dental Composite Restorations, Journal of dental research 96(4) (2017) 364-371.

[5] E.A.M. Kidd, Caries Diagnosis Within Restored Teeth, Advances in dental research 4(1) (1990) 10-13.

[6] M.S. Cenci, T. Pereira-Cenci, J.A. Cury, J.M. ten Cate, Relationship between Gap Size and Dentine Secondary Caries Formation Assessed in a Microcosm Biofilm Model, Caries research 43(2) (2009) 97-102.

[7] K. Diercke, A. Lussi, T. Kersten, R. Seemann, Isolated development of inner (wall) caries like lesions in a bacterial-based in vitro model, Clinical oral investigations 13(4) (2009) 439-444.

[8] N.K. Kuper, F.H. van de Sande, N.J. Opdam, E.M. Bronkhorst, J.J. de Soet, M.S. Cenci, M.C. Huysmans, Restoration materials and secondary caries using an in vitro biofilm model, Journal of dental research 94(1) (2015) 62-8.

[9] T.T. Maske, N.K. Kuper, M.S. Cenci, M. Huysmans, Minimal Gap Size and Dentin Wall Lesion Development Next to Resin Composite in a Microcosm Biofilm Model, Caries research 51(5) (2017) 475-481.

[10] H. Askar, F. Brouwer, M. Lehmensiek, S. Paris, F. Schwendicke, The association between loading of restorations and secondary caries lesions is moderated by the restoration material elasticity, Journal of dentistry 58 (2017) 74-79.

[11] D. Khvostenko, S. Salehi, S.E. Naleway, T.J. Hilton, J.L. Ferracane, J.C. Mitchell, J.J. Kruzic, Cyclic mechanical loading promotes bacterial penetration along composite restoration marginal gaps, Dental materials : official publication of the Academy of Dental Materials 31(6) (2015) 702-10.

[12] N.K. Kuper, N.J. Opdam, E.M. Bronkhorst, J.L. Ruben, M.C. Huysmans, Hydrodynamic flow through loading and in vitro secondary caries development, Journal of dental research 92(4) (2013) 383-7.

[13] K.S. Vandewalle, J.L. Ferracane, T.J. Hilton, R.L. Erickson, R.L. Sakaguchi, Effect of energy density on properties and marginal integrity of posterior resin composite restorations, Dental materials : official publication of the Academy of Dental Materials 20(1) (2004) 96-106.

[14] Y. Liu, L. Tjaderhane, L. Breschi, A. Mazzoni, N. Li, J. Mao, D.H. Pashley, F.R. Tay, Limitations in bonding to dentin and experimental strategies to prevent bond degradation, Journal of dental research 90(8) (2011) 953-68.

[15] L. Tjaderhane, Dentin bonding: can we make it last?, Operative dentistry 40(1) (2015) 4-18.

[16] F.F. Demarco, K. Collares, M.B. Correa, M.S. Cenci, R.R. Moraes, N.J. Opdam, Should my composite restorations last forever? Why are they failing?, Brazilian oral research 31(suppl 1) (2017) e56.

[17] I.A. Mjor, Frequency of secondary caries at various anatomical locations, Operative dentistry 10(3) (1985) 88-92.

[18] I.A. Mjor, Clinical diagnosis of recurrent caries, Journal of the American Dental Association (1939) 136(10) (2005) 1426-33.
[19] N.K. Kuper, N.J.M. Opdam, J.L. Ruben, J.J. de Soet, M.S. Cenci, E.M. Bronkhorst, M.C.D.N.J.M. Huysmans, Gap Size and Wall Lesion Development Next to Composite, Journal of dental research 93(7_suppl) (2014) 108S-113S.
[20] N.K. Kuper, N.J. Opdam, E.M. Bronkhorst, M.C. Huysmans, The influence of approximal restoration extension on the development of secondary caries, Journal of dentistry 40(3) (2012) 241-7.
[21] N.J. Opdam, E.M. Bronkhorst, J.M. Roeters, B.A. Loomans, A retrospective clinical study on longevity of posterior composite and amalgam restorations, Dental materials : official publication of the Academy of Dental Materials 23(1) (2007) 2-8.
[22] F.H. van de Sande, N.J. Opdam, P.A. Rodolpho, M.B. Correa, F.F. Demarco, M.S. Cenci, Patient risk factors' influence on survival of posterior composites, Journal of dental research 92(7 Suppl) (2013) 78s-83s.
[23] F.F. Demarco, K. Collares, F.H. Coelho-de-Souza, M.B. Correa, M.S. Cenci, R.R. Moraes, N.J.M. Opdam, Anterior composite restorations: A systematic review on long-term survival and reasons for failure, Dental Materials 31(10) (2015) 1214-1224.
[24] M.B. Correa, M.A. Peres, K.G. Peres, B.L. Horta, A.J. Barros, F.F. Demarco, Do socioeconomic determinants affect the quality of posterior dental restorations? A multilevel approach, Journal of dentistry 41(11) (2013) 960-967.
[25] M. Laske, N.J.M. Opdam, E.M. Bronkhorst, J.C.C. Braspenning, M.C.D.N.J.M. Huysmans, Longevity of direct restorations in Dutch dental practices. Descriptive study out of a practice based research network, Journal of dentistry 46 (2016) 12-17.
[26] F.F. Demarco, M.B. Correa, M.S. Cenci, R.R. Moraes, N.J. Opdam, Longevity of posterior composite restorations: not only a matter of materials, Dental materials : official publication of the Academy of Dental Materials 28(1) (2012) 87-101.
[27] F. Schwendicke, H. Kruger, P. Schlattmann, S. Paris, Restoration outcomes after restoring vital teeth with advanced caries lesions: a practice-based retrospective study, Clinical oral investigations 20(7) (2016) 1675-81.
[28] F. Brouwer, H. Askar, S. Paris, F. Schwendicke, Detecting Secondary Caries Lesions: A Systematic Review and Meta-analysis, Journal of dental research 95(2) (2016) 143-51.
[29] I.A. Mjor, J.E. Moorhead, J.E. Dahl, Reasons for replacement of restorations in permanent teeth in general dental practice, International dental journal 50(6) (2000) 361-6.
[30] I.A. Mjor, C. Shen, S.T. Eliasson, S. Richter, Placement and replacement of restorations in general dental practice in Iceland, Operative dentistry 27(2) (2002) 117-23.
[31] F. Schwendicke, F. Brouwer, S. Paris, M. Stolpe, Detecting Proximal Secondary Caries Lesions: A Cost-effectiveness Analysis, Journal of dental research 95(2) (2016) 152-9.
[32] H. Askar, Y.K. Tu, S. Paris, Y.C. Yeh, F. Schwendicke, Risk of caries adjacent to different restoration materials: Systematic review of in situ studies, Journal of dentistry 56 (2017) 1-10.
[33] C. Boutsiouki, R. Frankenberger, S. Lucker, N. Kramer, Inhibition of secondary caries in vitro by addition of chlorhexidine to adhesive components, Dental materials : official publication of the Academy of Dental Materials 35(3) (2019) 422-433.
[34] F. Hetrodt, J. Lausch, H. Meyer-Lueckel, G. Conrads, C. Apel, Evaluation of Restorative Materials Containing Preventive Additives in a Secondary Caries Model in vitro, Caries research (2019) 1-10.

[35] G.S. do Amaral, T. Negrini, M. Maltz, R.A. Arthur, Restorative materials containing antimicrobial agents: is there evidence for their antimicrobial and anticaries effects? A systematic review, Australian dental journal 61(1) (2016) 6-15.
[36] F. Schwendicke, G. Gostemeyer, M. Stolpe, J. Krois, Amalgam Alternatives: Cost-Effectiveness and Value of Information Analysis, Journal of dental research (2018) 22034518782671.
[37] F. Schwendicke, U. Blunck, Y.K. Tu, G. Gostemeyer, Does Classification of Composites for Network Meta-analyses Lead to Erroneous Conclusions?, Operative dentistry 43(2) (2018) 213-222.
[38] J.P.T. Higgins, Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.1. The Cochrane Collaboration, http://www.cochrane-handbook.org (2008).
[39] G. van Valkenhoef, G. Lu, B. de Brock, H. Hillege, A.E. Ades, N.J. Welton, Automating network meta-analysis, Research Synthesis Methods 3(4) (2012) 285-299.
[40] G. Salanti, J.P. Higgins, A.E. Ades, J.P. Ioannidis, Evaluation of networks of randomized trials, Stat. Methods Med. Res. 17(3) (2008) 279-301.
[41] G. Salanti, F.K. Kavvoura, J.P. Ioannidis, Exploring the geometry of treatment networks, Ann. Intern. Med. 148(7) (2008) 544-53.
[42] S. Dias, A.J. Sutton, A.E. Ades, N.J. Welton, Evidence synthesis for decision making 2: a generalized linear modeling framework for pairwise and network meta-analysis of randomized controlled trials, Medical decision making : an international journal of the Society for Medical Decision Making 33(5) (2013) 607-17.
[43] S.P. Brooks, A. Gelman, General Methods for Monitoring Convergence of Iterative Simulations, Journal of Computational and Graphical Statistics 7(4) (1998) 434-455.
[44] Y.K. Tu, I. Needleman, L. Chambrone, H.K. Lu, C.M. Faggion, Jr., A Bayesian network meta-analysis on comparisons of enamel matrix derivatives, guided tissue regeneration and their combination therapies, Journal of clinical periodontology 39(3) (2012) 303-14.
[45] G. Salanti, A.E. Ades, J.P. Ioannidis, Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial, Journal of clinical epidemiology 64(2) (2011) 163-71.
[46] B. Rouse, A. Chaimani, T. Li, Network meta-analysis: an introduction for clinicians, Internal and emergency medicine 12(1) (2017) 103-111.
[47] D. Jackson, J.K. Barrett, S. Rice, I.R. White, J.P. Higgins, A design-by-treatment interaction model for network meta-analysis with random inconsistency effects, Statistics in medicine 33(21) (2014) 3639-54.
[48] A. Chaimani, J.P. Higgins, D. Mavridis, P. Spyridonos, G. Salanti, Graphical tools for network meta-analysis in STATA, PloS one 8(10) (2013) e76654.
[49] I. Nedeljkovic, J. De Munck, V. Slomka, B. Van Meerbeek, W. Teughels, K.L. Van Landuyt, Lack of Buffering by Composites Promotes Shift to More Cariogenic Bacteria, Journal of dental research 95(8) (2016) 875-81.
[50] M. Laske, N. Opdam, E. Bronkhorst, J. Braspenning, M. Huysmans, Ten-Year Survival of ClassII Restorations Placed by General Practitioners, JDR Clinical & Translational Research 3 (2016) 292-9.
[51] N.J. Opdam, E.M. Bronkhorst, B.A. Loomans, M.C. Huysmans, 12-year survival of composite vs. amalgam restorations, Journal of dental research 89(10) (2010) 1063-7.
[52] J. Ferracane, T. Hilton, A. Korpak, J. Gillette, P.S. McIntyre, J. Berg, P. Northwest, Use of caries prevention services in the Northwest PRECEDENT dental network, Community Dentistry & Oral Epidemiology 39(1) (2011) 69-78.

[53] V.V. Gordan, J.L. Riley, 3rd, R.M. Carvalho, J. Snyder, J.L. Sanderson, M. Anderson, G.H. Gilbert, Methods used by Dental Practice-based Research Network (DPBRN) dentists to diagnose dental caries, Operative dentistry 36(1) (2011) 2-11.
[54] K. Elhennawy, H. Askar, P.G. Jost-Brinkmann, S. Reda, A. Al-Abdi, S. Paris, F. Schwendicke, In vitro performance of the DIAGNOcam for detecting proximal carious lesions adjacent to composite restorations, Journal of dentistry 72 (2018) 39-43.
[55] V.V. Gordan, Clinical evaluation of replacement of class V resin based composite restorations, Journal of dentistry 29(7) (2001) 485-8.
[56] V.V. Gordan, In vitro evaluation of margins of replaced resin-based composite restorations, J Esthet Dent 12(4) (2000) 209-15.
[57] V.V. Gordan, E. Mondragon, C. Shen, Replacement of resin-based composite: evaluation of cavity design, cavity depth, and shade matching, Quintessence international (Berlin, Germany : 1985) 33(4) (2002) 273-8.
[58] D. Green, L. Mackenzie, A. Banerjee, Minimally Invasive Long-Term Management of Direct Restorations: the '5 Rs', Dental update 42(5) (2015) 413-6, 419-21, 423-6.
[59] P. Kanzow, R. Hoffmann, C. Tschammler, J. Kruppa, T. Rödig, W. A, At**titudes, Practice and Experience of German Dentists Regarding Repair Restorations.**, Clinical oral investigations submitted (2016).
[60] V.V. Gordan, J. Riley, 3rd, S. Geraldeli, O.D. Williams, J.C. Spoto, 3rd, G.H. Gilbert, The decision to repair or replace a defective restoration is affected by who placed the original restoration: findings from the National Dental PBRN, Journal of dentistry 42(12) (2014) 1528-34.
[61] V.V. Gordan, J.L. Riley, S. Geraldeli, D.B. Rindal, V. Qvist, J.L. Fellows, H.P. Kellum, G.H. Gilbert, Repair or replacement of defective restorations by dentists in The Dental Practice-Based Research Network, The Journal of the American Dental Association 143(6) (2012) 593-601.
[62] N.J. Opdam, E.M. Bronkhorst, B.A. Loomans, M.C. Huysmans, Longevity of repaired restorations: a practice based study., Journal of dentistry for children (Chicago, Ill.) 40(10) (2012) 889-35.
[63] R.J. Smales, W.S. Hawthorne, Long-term survival of repaired amalgams, recemented crowns and gold castings, Operative dentistry 29(3) (2004) 249-53.
[64] J. Manhart, H. Chen, G. Hamm, R. Hickel, Buonocore Memorial Lecture. Review of the clinical survival of direct and indirect restorations in posterior teeth of the permanent dentition, Operative dentistry 29(5) (2004) 481-508.
[65] F. Schwendicke, G. Gostemeyer, U. Blunck, S. Paris, L.Y. Hsu, Y.K. Tu, Directly Placed Restorative Materials: Review and Network Meta-analysis, Journal of dental research (2016).
[66] P.A. Da Rosa Rodolpho, T.A. Donassollo, M.S. Cenci, A.D. Loguercio, R.R. Moraes, E.M. Bronkhorst, N.J. Opdam, F.F. Demarco, 22-Year clinical evaluation of the performance of two posterior composites with different filler characteristics, Dental materials : official publication of the Academy of Dental Materials 27(10) (2011) 955-63.
[67] M.O. Sharif, M. Catleugh, A. Merry, M. Tickle, S.M. Dunne, P. Brunton, V.R. Aggarwal, L.Y. Chong, Replacement versus repair of defective restorations in adults: resin composite, The Cochrane database of systematic reviews 2 (2014) Cd005971.
[68] P. Kanzow, A. Wiegand, F. Schwendicke, Cost-effectiveness of repairing versus replacing composite or amalgam restorations, Journal of dentistry 54 (2016) 41-47.
[69] B. Loomans, M. Ozcan, Intraoral Repair of Direct and Indirect Restorations: Procedures and Guidelines, Operative dentistry 41(S7) (2016) S68-S78.

[70] R. Hickel, K. Brushaver, N. Ilie, Repair of restorations--criteria for decision making and clinical recommendations, Dental materials : official publication of the Academy of Dental Materials 29(1) (2013) 28-50.
[71] I. Onisor, S. Bouillaguet, I. Krejci, Influence of different surface treatments on marginal adaptation in enamel and dentin, The journal of adhesive dentistry 9(3) (2007) 297-303.
[72] P. Angkasith, J.O. Burgess, M.C. Bottino, N.C. Lawson, Cleaning Methods for Zirconia Following Salivary Contamination, J Prosthodont 25(5) (2016) 375-9.
[73] E. Fernandez, J. Martin, P. Vildosola, O.B. Oliveira Junior, V. Gordan, I. Mjor, C. Bersezio, J. Estay, M.F. de Andrade, G. Moncada, Can repair increase the longevity of composite resins? Results of a 10-year clinical trial, Journal of dentistry 43(2) (2015) 279-86.
[74] J. Martin, E. Fernandez, J. Estay, V.V. Gordan, I.A. Mjor, G. Moncada, Minimal invasive treatment for defective restorations: five-year results using sealants, Operative dentistry 38(2) (2013) 125-33.
[75] V.V. Gordan, J.L. Riley, 3rd, P.K. Blaser, E. Mondragon, C.W. Garvan, I.A. Mjor, Alternative treatments to replacement of defective amalgam restorations: results of a seven-year clinical study, 142 (2011) 842-849.

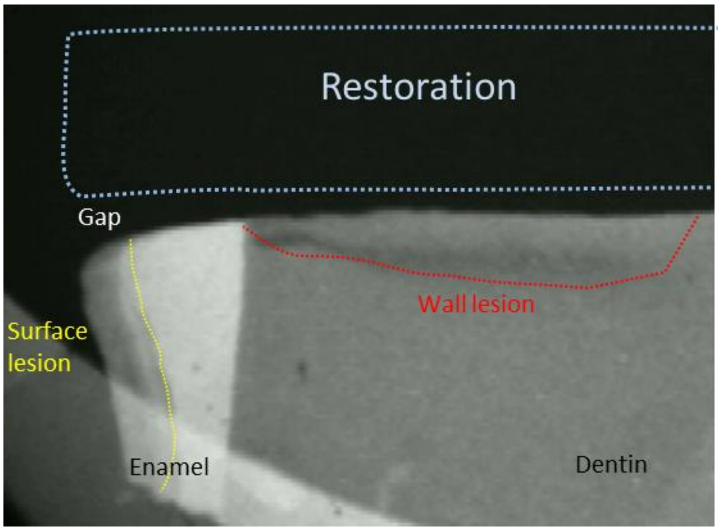

Figure 1: Typical cross-section through a “true” secondary carious lesion. A surface lesion and a wall lesion are present; the wall lesion extends along the interface between tooth and restoration material.

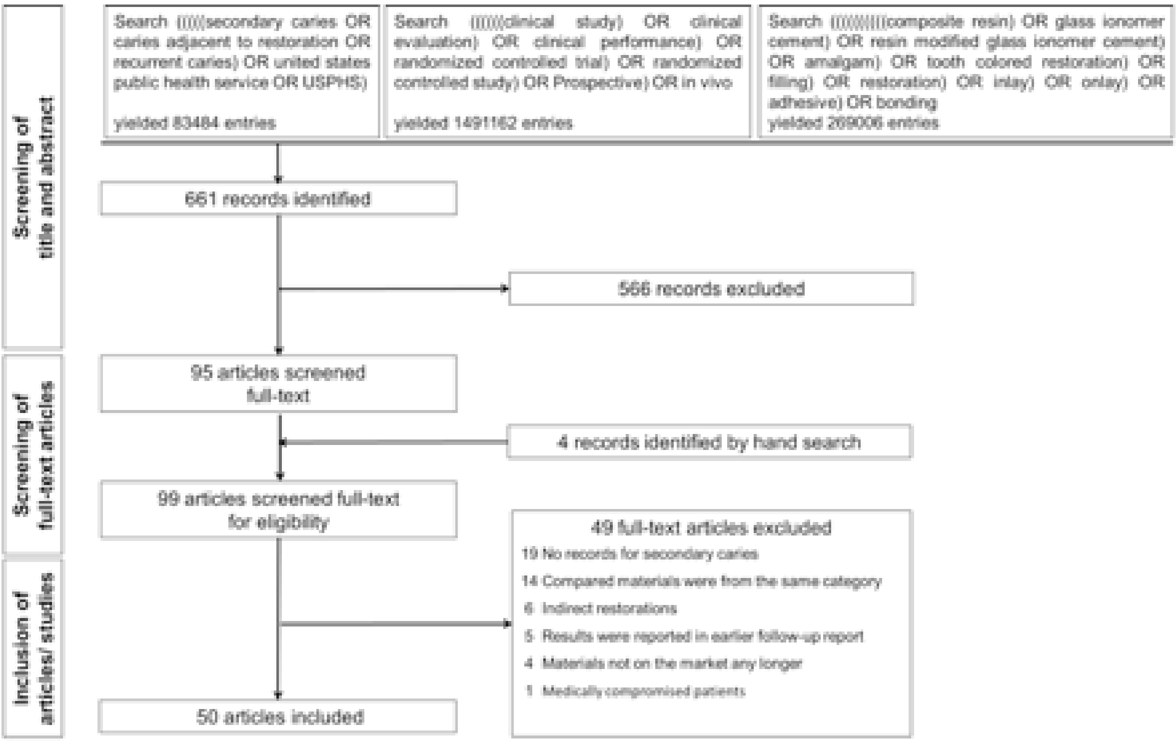

Figure 2: Flowchart of the review process

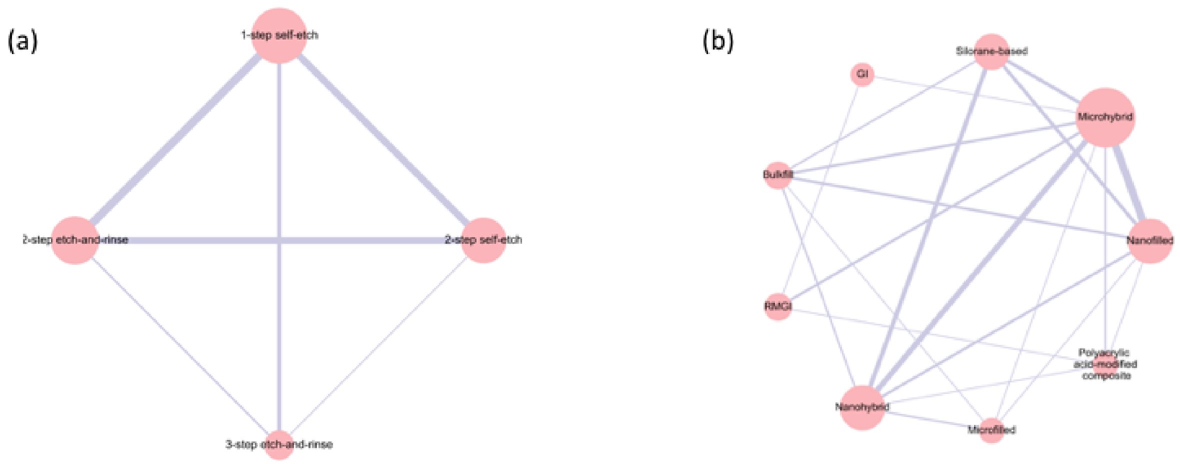

Figure 4: Network of compared adhesive strategies (a) and restorative materials (b). Nodes (red circles) and connections (blue lines) are used to display actually made pairwise comparisons. The size of the node indicates the number of studies testing this strategy; thickness of the lines indicates the number of studies in which exact comparison was made.

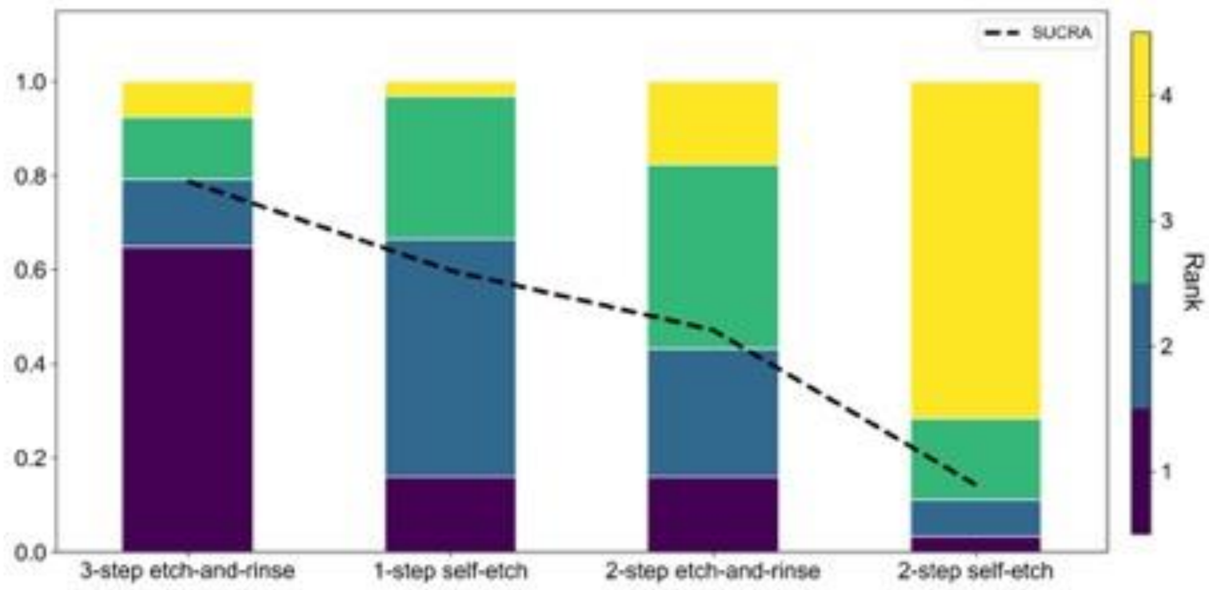

Figure 4: Cumulative ranks and SUCRA-values. Each adhesive strategy is represented by a unique bar. In the present study and using Bayesian network meta-analysis, the ranking of each adhesive strategy was estimated over a total of 80000 iterations (calculation rounds). For each iteration, each strategy received a rank; ranks are color-coded (dark blue: first rank, yellow: last rank). Each strategy hence received particular ranks in a certain number of iterations; the resulting frequency (in %) is displayed. A strategy can, for example, be ranked first in ca. 80% of these iterations (e.g. 3-step etch-and-rinse) indicating this strategy being likely ranked in the top tier, or can be ranked very differently in different iterations (e.g. 2-szep etch-and-rinse), with the bar having a wide range of colors, indicating large uncertainty. The strategies are ordered by their SUCRA-value (dotted line), SUCRA-values indicate the cumulative probability of being ranked first, second etc; high SUCRA-value indicate a low risk of secondary caries lesions.

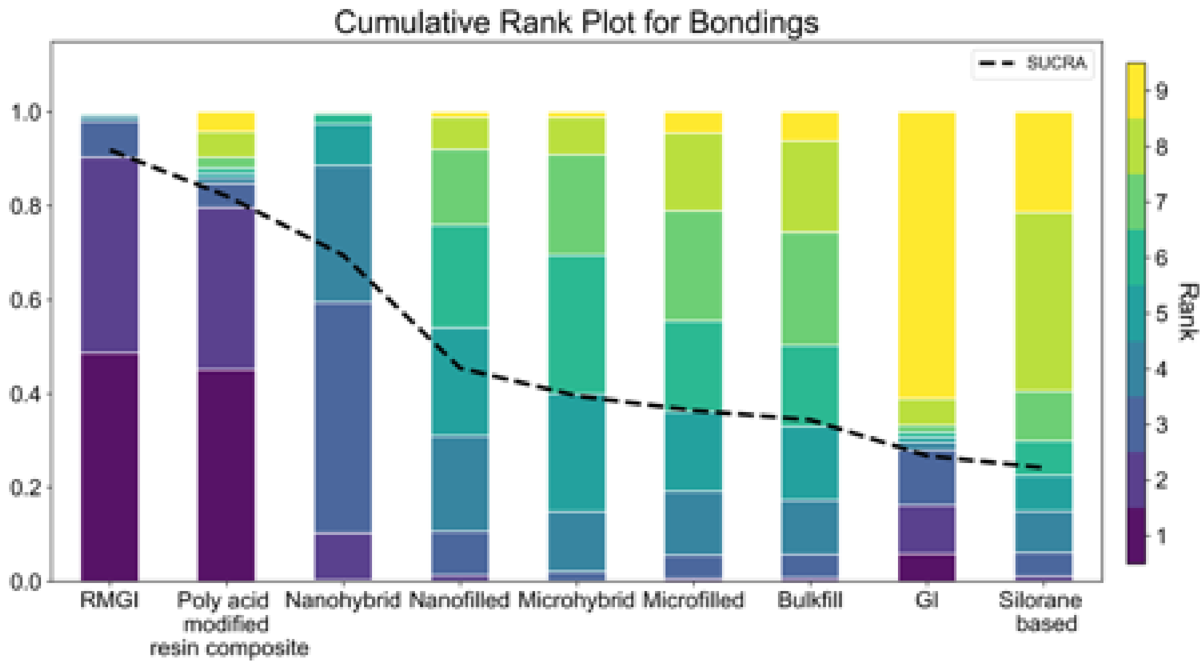

Figure 5: Cumulative ranks and SUCRA-values. Each restorative material is represented by a unique bar. In the present study and using Bayesian network meta-analysis, the ranking of each material was estimated over a total of 80000 iterations (calculation rounds). For each iteration, each material received a rank; ranks are color-coded (dark blue: first rank, yellow: last rank). Each material hence received particular ranks in a certain number of iterations; the resulting frequency (in %) is displayed. A material can, for example, be ranked first in ca. 50% and second in ca. 40% of these iterations (e.g. RMGI) indicating this material being likely ranked in the top tier, or can be ranked very differently in different iterations (e.g. nanofilled composites), with the bar having a wide range of colors, indicating large uncertainty. The materials are ordered by their SUCRA-value (dotted line), SUCRA-values indicate the cumulative probability of being ranked first, second etc; high SUCRA-value indicate a low risk of secondary caries lesions.

Tables

Table 1: Annual failure rates (AFR) in repaired versus replaced restorations, from [68].

Study	Sample size[1]	AFR[2] Repair	AFR Replacement	Relative Risk (RR)	Follow-up, restorations
Composite					
Opdam 2010, 2012 [51, 62]	113	5.7	1.8	3.2	5 years, „large posterior“
Fernandez 2015 [73]	23	2.2	0.4	5.5	10 years, class I and II
Martin 2013 [74]	14*	0.0	0.0	1	5 years, class I and II
Sample-size weighted mean				**3.4**	
Amalgam					
Gordan 2011 [75]	27	0.5	1.5	0.3	7 years, mainly class II
Smales and Hawthorne 2004 [63]	24	6.3	3.7	1.7	10 years, class II
Opdam 2010, 2012 [51, 62]	133	9.3	1.3	7.2	5 years, „large posterior“
Martin 2013 [74]	17*	0.0	0.0	1.0	5 years, class I and II
Sample-size weighted mean				**5.0**	

* Martin et al. 2013 only reported overall numbers of followed composites and amalgams. As 34% were repaired (the rest was replaced or left untreated), we reduced the sample size accordingly.

[1]Sample size of repair group only.
[2]The annual failure rate (AFR) was either used as reported, or estimated based on USPHS scores, with only categories Charlie and Delta counting as failure.