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Restorative Thresholds for Carious Lesions: Systematic Review/ Meta-analysis

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Running title: Dentists' Thresholds for Restorative Interventions of Carious Lesions

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Abstract

Current evidence supports non-invasive/non-restorative treatment of "early" carious lesions, i.e. those confined to enamel or reaching the enamel-dentin junction. The extent that dentists' thresholds for intervening restoratively have changed in line with this evidence is unknown. A systematic review to determine dentists' and therapists' current lesion threshold for carrying our restorative interventions in adults/children and primary/permanent teeth), was registered and carried out. Embase, Medline via PubMed, and Web of Science were searched for observational studies, without language, time or quality restrictions. Screening and data extraction were independent and in duplicate. Random-effects meta-analysis with subgroup and meta-regression analysis was performed. Thirty studies, mainly involving dentists, met the inclusion criteria. There was heterogeneity in the sampling frames, methods and scales used to investigate thresholds. The studies spanned 30 years (1983-2014) and sample representativeness and response bias issues were likely to have affected the results. Studies measured what dentists said they would do rather than actually did. Studies represented 17 countries, focussing mainly on adults (n=17) and permanent teeth (n=24). For proximal carious lesions confined to enamel (not reaching enamel-dentin junction), 21% (95% confidence interval [CI] 15;28) of dentists/therapists would intervene invasively. The likelihood of a restorative intervention almost doubled (risk ratio 1.98 [95%CI

1.68;2.33]) in high caries risk patients. For proximal lesions extending up to enamel-dentin junction, 47% (95%CI 39;55) of dentists/therapists would intervene restoratively. For occlusal lesions with enamel discoloration/cavitation, but no clinical/radiographic dentin involvement, 12% (95%CI 6;22) of dentists/therapists stated they would intervene, increasing to 74% (95%CI 56;86) with dentin involvement. There was variance between countries but no significant temporal trend. A significant proportion of dentists/therapists said they would intervene invasively (restoratively) on carious lesions where evidence and clinical recommendations indicate less invasive therapies should be used. There is great need to understand decisions to intervene restoratively and to find implementation interventions that translate research evidence into clinical practice.

Introduction

Previous understanding of dental caries as an infectious disease meant that lesion management was synonymous with carious tissue removal. However, contemporary understanding characterizes caries as a disease of imbalance in biofilm flora and activity, resulting in imbalance of de- and remineralization and does not support this aggressive symptomatic treatment. Increasing evidence endorses management by less invasive strategies to arrest lesions using biofilm removal, biofilm sealing-in strategies and remineralization treatments (Marinho et al. 2003; Marinho et al. 2013; Ricketts et al. 2013; Schwendicke et al. 2013a; Schwendicke et al. 2013b; Dorri et al. 2015; Innes et al. 2015).

Traditional approaches of removing tooth tissue affected by the caries process might have been justifiable when lesion progression from the outer aspect of enamel, through dentin, to the dental pulp, was relatively fast. In addition to the rate of caries progression being slower than was generally believed (Mejare 1999), wide availability of fluoride and intensive individual and public health efforts have promoted lesion arrest and slowed progression. The rates for carious lesions confined to enamel, transitioning to dentin lesions have been estimated to be in the order of 21 lesions/100 tooth surface-years for permanent molars (i.e only around 1 in 5 lesions can be expected to progress to reach dentin in a year) and 33 for primary molars (around 1 in 3 lesions progress to reach dentin within a year) (Mejare et al. 1999; Mejare 2001; Stenlund et al. 2002).

Given this limited risk of lesion progression and an increasing body of evidence supporting less interventive treatments, there is growing consensus that invasive (and largely restorative) interventions should be mainly restricted to treatment of cavitated non-cleansable lesions, having reached a stage where they can no longer be sealed or where restorations are required to restore aesthetics, structural integrity or function (Hobdell et al. 2003; Frencken et al. 2012; Schwendicke et al. 2016). For all other lesions, avoiding invasive treatments is likely to retain teeth for longer at lower costs, as expensive and even more invasive re-treatments are postponed or even avoided (Schwendicke et al. 2014; Schwendicke et al. 2015a; Schwendicke et al. 2015b). This is of great relevance considering the global clinical and economic burden stemming from dental caries (Kassebaum et al. 2015; Lisl et al. 2015).

There is conflicting evidence around how well dentists' restorative care planning behaviour aligns to these recommendations, especially for managing carious lesions limited to enamel or the outer aspect of dentin (Schwendicke et al. 2015c). We aimed to systematically appraise this evidence, evaluate variability in intervention thresholds between countries, and investigate factors influencing this. As well as identifying gaps and weaknesses in the literature and informing future studies, this may help develop strategies to reduce intervention levels by identifying areas of good practice which can be further investigated.

Our primary objective was to answer the question: What are dentists' and dental therapists' thresholds for carrying out restorative interventions in adults or children (primary and permanent teeth) for proximal and occlusal carious lesions? Our secondary objectives were to assess whether these thresholds differed between countries, patient groups, or has changed over time and whether factors such as dentist's sex, patient age, socio-economic status, caries risk, tooth, primary or permanent dentition influenced dentists' thresholds?

Methods

The review protocol published in PROSPERO (01/04/2016) http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016038625.

Eligibility criteria

Study eligibility:

- observational peer reviewed studies without language, time or quality restrictions;
- reporting on dentists' or therapists' (including students) thresholds (clinically, radiographically or using other caries detection tools) for carrying out restorative interventions on carious lesions, for adults or children and in primary or permanent dentitions.

We searched Embase, Medline via PubMed, and Web of Science. The reference lists of identified full-texts were screened and cross-referenced. The search strategy was broad to maximize study capture as the key words might not be easily detected. The following three search areas were developed for each database and combined:

- ((((((restorative) OR restoration) OR invasive) OR drilling) OR cutting) OR filling) AND
- (((((decision) OR threshold) OR cut-off) OR intervene) OR survey) OR questionnaire AND
- (((caries) OR carious) OR decay) OR white spot

Both authors independently screened titles, compared findings and included full texts where there was disagreement. Full texts were assessed independently after de-duplication. Studies were included after agreement, with consensus being reached through discussion.

The following data items were extracted independently by both reviewers using piloted spreadsheets and discrepancies resolved through discussion:

- author names, survey year, publication year;
- dentists' and therapists' characteristics (country and other demographics), sampling frame, response rate (to help gauge representativeness, level of response and response bias);
- scenario: lesion classification system, primary/ permanent teeth, adults/ children;
- number of dentists using a specific threshold per overall sample of dentists; and
- additional factors assessed and might influence decision making (e.g. patient caries risk status).

Data synthesis

For the primary outcome, data from different studies on dentists' or therapists' treatment level thresholds were compared, with further assessment of thresholds per different countries/regions (see below), and publication years. If only data subgroups (e.g. different age groups) were available, we calculated the mean proportion of dentists or therapists intervening at different thresholds over these subgroups to avoid unit of analysis issues. Whilst it is an important point to see if there are any changes in practice over time, it is unlikely, without a large number of studies and repeated measures at different timepoints that it will be possible to detect these changes.

We pre-specified a number of subgroup analyses in our protocol. However, not all could be carried out:

- Subgroup analysis for carious lesion depths. We pooled different intervention depths into two thresholds.
    - Proximal surfaces, where intervention was in lesions (clinically or radiographically) (1) confined to enamel (E1, E2 – outer or inner half of enamel), (2) confined to enamel or extending up to enamel dentin junction (E1, E2, EDJ);
    - Occlusal lesions where intervention was in lesions (1) confined to the enamel and (2) confined to enamel or in outer dentin.
- High and low caries risk sub-groups were compared with each other where data were available.
- The countries that studies were carried out in were grouped according to region (North America, South America, Western Europe, Eastern Europe, Scandinavia, Australasia), to reflect similarities in dental teaching philosophies and, as far as possible, remuneration systems. No studies from Africa were identified. Some studies were carried out across different countries and results were split to reflect country, so that each data point related to the country rather than the study;
- Primary/permanent dentitions. Only two studies included primary dentition so subgroup analysis was not possible.
- Similarly for patients' socio-economic status or dentist's sex, there was insufficient data for analyses.

Meta-analysis of the proportion of dentists intervening at specific thresholds was performed using Comprehensive Meta-Analysis 2.2.064 (Biostat, NJ, USA). Heterogeneity was assessed using I^2-statistic (Higgins and Thompson 2002). Since heterogeneity was mostly found to be substantial (I^2>50%), a random-effect model was used for meta-analysis. Publication or reporting bias was evaluated using Funnel Plots and the Egger regression intercept test (Egger et al. 1997). Comparison of subgroups was by testing for heterogeneity across subgroups of categorical variables (Higgins et al. 2002; Borenstein and Higgins 2013). Random-effects meta-regression was used to evaluate the association between continuous variables and our outcome parameter.

Confidence in data

The studies were categorised for type then assessed and graded for quality based on the Newcastle Ottawa scoring tool (Wells et al. 2008). The tool was adapted for cross-sectional survey studies (detailed in Appendix 1a). Differences in reviewers' grading were resolved by consensus.

Results

From 136 identified studies, 30 studies (Appendix 2) with 18,135 participants met the inclusion criteria (Figure 1) and data were extracted (Appendix 3a and 3b). Sixteen studies were published within the last 10 years, three between 10 and 15 years ago and 11 studies were published more than 15 years ago. The studies were published

between 1985 and 2016 (mean 2004). The years of survey conduct were reported as ranging from 1983 to 2014, but were not reported for 11 studies. We were able to obtain all full-texts so did not need to contact study authors. The studies were scored using the modified Newcastle Ottawa Scale (Appendix 1b) with score range 2 to 6 (median=5; mode=5). No studies were high quality, 24 were moderate (scoring 4 to 6 points), and the remaining four studies were low quality.

Clinician participant characteristics

Twenty eight studies investigated dentists (95% of the sample n=17,121), one also investigated dental therapists (1%; n=247) and two examined dental students (4%; n=767). 21 of 28 studies involved general dental practitioners (GDPs), two included GDPs and specialists (restorative, paediatric and unspecified), one investigated operative dentistry teachers and one university teachers. Four studies did not specify dentist/clinician characteristics.

Sampling Frames and Samples

Random, stratified, convenience and inclusive sampling frames were all used. Of the 30 studies, 11 sampled nationwide, 10 at regional or state level, five at local level, three sampled dentists from different countries (with sampling mixed at nationwide and regional levels) and in one study the sampling frame level was not clear. Participants were selected at random or in such a way as to be relatively representative of the population being investigated (whether that was national, statewide or local) in 27 of the studies with a mean response rate of 69% (range 11-99%). In 10 of the 11 studies with nationwide representation, there was random participant selection. The mean response rate was 69% (range 38% to 93%). Six studies involved random selection of clinicians from regions and 12 included non-random selection or convenience sampling of practice based research networks or other selected groups (teachers or students). Selection was unclear in one study.

A wide range of countries (n=17 different countries) were represented (some in multiple studies). The 10 national level studies carried out at national level were conducted in France, Kuwait, Netherlands, Norway, Scotland (UK) and Sweden. The 11 state- or region-wide studies were set in Australia, Brazil, Canada, Croatia, Denmark, Iran, Japan, Norway, Scotland, Sweden, USA, 2 were local (Mexico and Israel). The three 'mixed' studies were carried out in Norway, Sweden, Denmark and the USA. In these studies, some countries' dentists were sampled at nationwide level and others at individual state level.

Clinical characteristics of the patients/teeth/ lesion locations

Most studies focussed on adult patients (n=15), three specifically on children, three on both adults and children separately and in nine studies it was implied that these were adults. Twenty eight studies looked at decisions on when to intervene in permanent teeth and two studies looked at primary and permanent teeth. Most studies (n=27) investigated thresholds for proximal lesions and 12 occlusal lesions, with nine of these looking at both.

A variety of methods were used to present lesion extent and investigate thresholds (Appendix 4):

- Dentists' thresholds for occlusal lesions were assessed using photographs of teeth in nine studies, written descriptions in two studies and extracted teeth embedded in resin blocks in one. All studies using clinical photographs employed identical sets of photographs and used the same 5-point scale.
- For proximal lesions, a wider variety of assessments was used: Diagrams in 15 studies, written description of radiographs in six, clinical radiographic images in four, radiographs of extracted teeth in one, and the system was unclear in one study. Furthermore, different scales were used for lesion classification and threshold decisions, ranging from one study using a two point scale to 12 studies using six point scales. Other scales: three points (n=2 studies), four points (n=3) and five points (n=9). Even for the most commonly used scale (Espelid et al. 2001) there was variability with some studies using a 5 point version and others used a 6-point version.

Dentists' restorative intervention thresholds for proximal lesions

Overall, 21% (95% confidence interval [CI] 15;28) of dentists or dental therapists, in 28 studies, stated they would intervene when the carious lesion was confined to enamel (had not reached the EDJ) (Figure 2a). There were statistical signs of publication bias ($p<0.05$/Egger), which were confirmed using funnel plot inspection (Appendix 5a). Heterogeneity was high (I^2=98%), with large variation in proportions between countries. Dentists from Scandinavian countries were statistically significantly less likely to intervene at this stage than dentists from other regions (p=0.02). Six studies compared the proportions of clinicians intervening on proximal lesions confined to enamel in high versus low risk populations, with dentists being 1.98 (95%CI 1.68;2.33) times more likely to intervene in high risk groups (Figure 2b). Global meta-regression did not find any significant trend of this proportion changing with time (p=0.555). When only pooling studies published within the last 15 years (17 studies) and 10 years (15 studies), there was very little change in the proportion of dentists or dental therapists stating they would intervene for lesions confined to enamel; 24% (95%CI 17;34) and 27% (95%CI18;37) respectively.

A higher proportion of dentists (47% [95%CI 39;55]) would intervene on proximal lesions extending up to the EDJ (27 studies), (Figure. 3). There were no signs of publication bias (Appendix 5b). Heterogeneity was high (I^2=98%), with a large, although non-significant, variation in the proportions between countries (p=0.09). Global meta-regression found the proportion to decrease over time (R^2=-3% [-7;0], p=0.05). When the analyses were limited to studies from the last 15 years (16 studies) and 10 years (14 studies), there was again little change; 46% (95%CI 34;58) and 44% (95%CI 32;758).

No studies investigated dentists intervening at this threshold in high versus low caries risk patients.

Dentists' restorative intervention thresholds for occlusal lesions

For occlusal lesions with enamel discoloration or cavitation, but no clinical or radiographic dentin involvement, 12% (95%CI 6;22) of dentists or dental therapists, in 10 studies, stated they would intervene invasively (Figure 4a). There were no indications of publication bias (Appendix 5c). Global meta-regression did not reveal any significant trend in this proportion (p=0.260). Heterogeneity was high (I^2=98%), with a large but non-significant

variation in the proportions between countries (p=0.392). When the data analysis was limited to only studies from the last 15 years (eight studies), there was very little change with 12% (95%CI 7;20) stating they would intervene. This remained similar when the data analysis was restricted to the last 10 years (six studies); 13% (95%CI 6;25).

Dentists were 2.46 (1.94;3.00) times more likely to intervene in high than low caries risk groups (Figure 4b).

For occlusal lesions clinically and/or radiographically involving dentin, 74% (95%CI 56;86) of dentists or dental therapists, in 10 studies, stated they would intervene (Figure 5a). There was no indication of publication bias (Appendix 5d). Global meta-regression did not reveal any significant trends in this proportion (p=0.289). Heterogeneity was high (I^2=98%), with a large but non-significant variation in proportions between countries (p=0.656). When the data analysis was limited to only studies from the last 15 years (eight studies), there was very little change in the proportion of dentists or dental therapists stating they would intervene; 76% (95%CI 65;83) and when restricting to the last 10 years (six studies); 74% (73;76).

Dentists were 1.49 (95%CI 1.37;1.62) times more likely to intervene in high than low risk groups (Figure 5b).

Discussion

Moves away from interventive management of carious lesions confined to enamel have been driven by evidence and recommended repeatedly for over 15 years (Tyas et al. 2000; Kidd and Fejerskov 2013; Schwendicke et al. 2016). Based on 30 observational, survey-based studies from 17 different counties and including 18,135 practitioners (mainly dentists), this systematic review shows a large proportion (21% for proximal lesions and 12% for occlusal lesions) of practitioners still using a “drill and fill” approach for enamel lesions. Furthermore, nearly half of surveyed practitioners would intervene on proximal lesions extending up to the EDJ, which is increasingly difficult to justify given the majority of these lesions are not cavitated and management options like sealing or infiltrating having been shown to successfully arrest the large majority of such lesions (Fontana et al. 2014; Dorri et al. 2015).

Reasons underlying this gap between evidence and dental practice have been investigated and discussed (Clarkson et al. 2008; Bonetti and Clarkson 2016; Innes et al. 2016; Schwendicke and Göstemeyer 2016). In this case, where diagnosis plays a part in decision making, the intuitive and often erroneous belief that early intervention is always beneficial (Moynihan et al., 2013) is fueled by the ever increasing number of highly sensitive detection tools being marketed and available, without sufficient emphasis on the often associated reduction in specificity (Bader et al. 2001, Schwendicke et al. 2015d) and risk of harm and adverse side effects (Schwendicke et al. 2015b). Another factor is the education of dentists and associated rationale as to why carious lesions are treated at all (Schwendicke and Göstemeyer 2016). We ascribe the differences seen in Scandinavian dentists who were significantly less interventional, partially for this reason. Given that one could expect global cariology teaching to have adopted a less invasive, evidence-based management of “early” carious lesions (Schulte et al. 2011; Splieth et al. 2011), it is surprising not to detect a reduction over time in the proportion of dentists intervening on enamel lesions. However, it could well be, that the large number of different countries

sampled over time, at different sampling levels (regional, local etc.) with different methodology (scenarios, threshold levels), might have masked any trend. Repeated cross-sectional data from single countries with similar sampling frames and methods are needed. Further reasons (for which there was insufficient data to assess) might include conforming to social norms (Kay et al. 1992; Schwendicke and Göstemeyer 2016) and organizational aspects (e.g. remuneration systems or healthcare philosophies.). Dentists' age was one possible factor underlying treatment decisions although the findings were ambiguous: younger dentists were more likely to intervene in enamel in one study (el-Mowafy et al. 1994), and older ones in another (Tveit et al. 1999).

Some studies also investigated factors moderating thresholds. Besides moderators external to the clinical decision maker (such as improved diagnostic tools and the healthcare framework), there are also internal moderators, which depend on the clinicians' perspective. This is clearly seen in this dataset. Early intervention was around twice as likely to be chosen for lesions in high caries risk patients compared with low risk. Whether or not this is justified or whether these patients are still entitled to, or likely to adopt, preventive practices remain unanswered questions. A similar moderation might be expected for the dentition (primary or permanent) or patient's age, but there was insufficient data to analyse these.

This study, and the underlying dataset has a number of limitations. Firstly, the sampled populations are likely to be biased to a certain extent by selection; additionally, samples were often small and only around a third of them at a national level. Although the majority of studies (27/30) attempted to include representative samples through random selection of participants, the risk of selection bias is especially high in samples yielded from dental practice board lists etc and response bias was also likely to have affected the sample. The effect of selection bias was not quantifiable. Secondly, all apart from two of the surveys (Kay et al. 1992; Fellows et al. 2014) were based on individual clinicians' report rather than through observational data collection, adding further risk of bias. Thirdly, our handling of the dataset involved having to make somewhat arbitrary decisions over how to group the studies. We chose geographical area because of the perception of less- and more- invasive philosophies being followed in different regions resulting from different teaching philosophies. It is notable that only 2% of Scandanavian dentists stated they would intervene when a carious lesion was confined to enamel (compared to 21% for all clinicians surveyed) and only 9% would intervene when lesions extended to the EDJ (compared to 47% of all clinicians). Fourthly, the studies were conducted over 30 years (16 of them within the last 10 years), with methodology evolving and data collection tools changing (with the lesion extent, for example, being depicted using diagrams, written descriptions, stylised radiographs and actual clinical data). However, pooling only studies published in the last 15 years and even 10 years had very little effect. For proximal lesions confined to enamel for all studies (up to 30 years) 21% of the clinicians said they would intervene, limited to the last 15 years this was 24% and limited to the last 10 years it was 27%. For proximal lesions up to the EDJ, all studies; 47% would intervene, limited to the last 15 years this was 46% and to the last 10 years it was 44%. There was even less change for occlusal lesions (although there were less studies). For occlusal lesions with enamel discoloration or cavitation, including all studies; 12% would intervene, limiting to the last 15 years, it remained

at 12% and when limiting to the last 10 years, 13%. For occlusal lesions clinically and/or radiographically involving dentin, 74% would intervene, including only studies from the last 15 years; 76% and for the last 10 years; 74%. The lack of, or minimal changes indicates that very little has changed in dentists thresholds for deciding to intervene compared to 15 or even up to 30 years ago. Finally, we excluded studies mixing diagnostics and thresholds, as the effect of interpretation of clinical/radiographic findings could have distorted clinicians' viewpoints and self-reports of behaviour. In a clinical setting, however, decision making is based on diagnostic assessment, which could be guided by beliefs underlying the overall approach towards managing carious lesions. Future studies should also employ qualitative methods for studying reasons for dentists making certain decisions (Schwendicke et al. 2015d), and should also consider a wider range of documents like clinical practice guidelines to not only measure, but understand these decisions.

Conclusions

Based on the findings of this review and within the data's limitations (sample representativeness, response bias and long time period covered), a significant proportion of dentists or dental therapists said they would intervene invasively (restoratively) for carious lesions which were clinically and/or radiographically confined to enamel or only minimally extended into dentin. This proportion varied greatly between countries and was further influenced by the individual patient's caries risk profile. This data is historical and there is great need to understand the current status and the decision-making process to facilitate translation of research evidence into clinical practice and reduce over-treatment.

Contributions

NI and FS jointly conceived the study, drafted the manuscript, contributed to the development of the selection criteria, the search strategy, the risk of bias assessment strategy and data extraction criteria. FS provided statistical expertise. FS and NI provided expertise on caries management. Both authors wrote, critically revised and approved the final manuscript.

Support and Conflict of Interests

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Figure 1. Flow chart of identification, screening and assessing studies for inclusion eligibility. From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure 2. Dentists intervening invasively (restoratively) at E1/E2 level for proximal carious lesions. (a) The proportion of dentists (95% CI) is shown by region and year. Open diamonds are subtotals and full diamonds indicate total proportions. I^2 indicates heterogeneity. (b) The relative ratios of proportion of dentists intervening in high versus low caries risk status.

Figure 3. Dentists intervening invasively (restoratively) at E1/E2/EDJ level for proximal carious lesions by region and year. The proportion (95% CI) of dentists is shown; open diamonds are subtotals and full diamonds indicate total proportions. I^2 indicates the heterogeneity.

Figure 4. Dentists intervening invasively (restoratively) in occlusal carious lesions clinically and/or radiographically confined to enamel. (a) The proportion of dentists (95% CI) is shown by region and year. Open diamonds are subtotals and full diamonds indicate total proportions. I^2 indicates the heterogeneity. (b) The relative ratios of proportion of dentists intervening in high versus low caries risk status.

Figure 5. Dentists intervening invasively (restoratively) in occlusal carious lesions clinically and/or radiographically involving enamel and/or dentin. (a) The proportion of dentists (95% CI) is shown by region and year. Open diamonds are subtotals and full diamonds indicate total proportions. I^2 indicates the heterogeneity. (b) The relative ratios of proportion of dentists intervening in high versus low caries risk status.

Appendix 1a. Modified Newcastle-Ottawa Scale adapted for cross-sectional survey studies

Appendix 1b. Modified Newcastle-Ottawa Scale scores for included studies.

Appendix 2 Included studies

Appendix 3 Data extraction table

Appendix 4. Different threshold grading systems used in studies

Appendix 5. Funnel Plots

(a) Standard errors of estimates from different studies plotted on the logit proportion of dentists intervening invasively (restoratively) at E1/E2 level for proximal carious lesions. An asymmetric distribution of studies indicates publication bias.

(b) Standard errors of estimates from different studies plotted on the logit proportion of dentists intervening invasively (restoratively) at E1/E2/EDJ level for proximal lesions. An asymmetric distribution of studies indicates publication bias.

(c) Standard errors of estimates from different studies plotted on the logit proportion of dentists intervening invasively (restoratively) for occlusal carious lesions confined to enamel.

(d) Standard errors of estimates from different studies plotted on the logit proportion of dentists intervening invasively (restoratively) for occlusal lesions clinically and/or radiographically involving enamel and/or dentin.