[Dentistry] Brush Your Teeth Twice Daily — The Evidence Behind (choxos.medium.com)

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The following assessments are for this article:

Kumar S, Tadakamadla J, Johnson NW. Effect of Toothbrushing Frequency on Incidence and Increment of Dental Caries: A Systematic Review and Meta-Analysis. *Journal of Dental Research*. 2016;95(11):1230-1236. doi:10.1177/0022034516655315.

1 Assessing the certainty of evidence

For the following PECO question:

- **P**opulation: All ages
- **E**xposure: Frequent toothbrushing (at least once daily on average)

- **C**omparison: Infrequent toothbrushing (less than once daily on average)
- **O**utcome: Incidence of dental caries

All the assessments are based on the data reported by the authors. I didn't do any new analysis and trusted on the data provided by the authors.

GRADE domain	Rating	Reasons
Risk of Bias	Not serious	Studies with the most weights in meta-analysis (Vanobbergen 2001, Hausen 1981, and Bernabe 2012) are of high quality in selection bias and overall (Appendix Table 4). Also, meta-regression shows that overall quality of the studies had negligble influence on the results of the meta-analysis. Therefore, it's unlikely that the results of meta-analysis was influenced by risk of bias of the included studies and we can conclude that bias is not a serious concern for this outcome.
Inconsistency	Not serious	There are variations in point estimates across studies, and confidence intervals do not entirely overlap. The I^2 value is not large, however (31%, P=0.12). The heterogeneity can be explained by subgroups since I^2=0 in the second subgroup of the meta-analysis. But the heterogeneity in the first subgroup still exists, though not high (45%, P=0.07). Therefore, there are no serious concerns in this domain.
Indirectness	Not serious	The majority of the studies were conducted among <18-year-olds. Exposure and outcome aligns with our question of interest. However, studies were different in sample size, follow-up period, and caries diagnosis level (cavitated or non-cavitated). The meta-regression results in Appendix Table 5 shows that these factors were not influential. The third meta-analysis in Figure 4 also shows that the results were similar for decidiuous and permanent dentitions (Odds: 1.75 vs 1.39) which can imply that the effect of age was also negligible. So, we can conclude no serious concerns for this domain.
Imprecision	Not serious	The sample size is not shown in the forest plot but a quick glance at Appendix Table 3 confirms that the number of participants in the meta-analysis is higher than the optimal information size. The confidence interval doesn't cross the null value (1.50, 95% CI: 1.34–1.69). Therefore, there are no serious concerns in this domain.
Publication bias	Undetected	We have a sufficient number of studies to assess publication bias through a funnel plot (more than the minimum of 10). The funnel plot (Figure 5) does not appear to be asymmetric and, in fact, includes some studies on the left-hand side, which does not favour frequent toothbrushing. Additionally, they conducted a comprehensive search across multiple sources (Medline, EMBASE, Cochrane CENTRAL, and CINAHL from database inception). They also captured small studies with small effects. Therefore, we can say publication bias is undetected in this case.

1.1 Overall certainty of evidence

Since this meta-analysis includes observational studies, the certainty of evidence starts with "Low". The effect doesn't seem to be large (OR=1.50), and there is no dose-response gradient (between 1 and 2 thresholds). Therefore, the overall certainty of evidence remains to be **Low**.

2 Quality of the review

Using AMSTAR 2 checklist.

Domain	Response	Reason
1. Did the research questions and inclusion criteria for the review include the components of PICO?	Yes	
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	**No**	There is no mention of prior registration in PROSPERO or any other places. Searching in PROSPERO also led to no results.
3. Did the review authors explain their selection of the study designs for inclusion in the review?	Yes	"Case-control, prospective cohort, retrospective cohort, and experimental trials that evaluated the effect of toothbrushing frequency on the incidence or increment of new carious lesions were considered for inclusion."
4. Did the review authors use a comprehensive literature search strategy?	**No**	Publication restrictions without proper justification: • Language: English only; • Time: From 1980: "There were very few longitudinal studies published prior to 1980 on this topic, and it proved difficult to retrieve full texts of these articles and even abstracts in many instances."

Domain	Response	Reason
5. Did the review authors perform study selection in duplicate?	Yes	"Screening of titles and abstracts was performed by 2 independent reviewers (S.K. and J.T.)."
6. Did the review authors perform data extraction in duplicate?	Yes	"Data extraction from the full texts of the articles was independently performed by 2 reviewers (S.K. and J.T.)."
7. Did the review authors provide a list of excluded studies and justify the exclusions?	Yes	Appendix Table 2.
8. Did the review authors describe the included studies in adequate detail?	Yes	Appendix Table 3.
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	Partial Yes	The tool they used (Effective Public Health Practice Project's Qualitative Assessment Tool for Quantitative Studies) doesn't include a domain for "selection of the reported result from among multiple measurements or analyses of a specified outcome".
10. Did the review authors report on the sources of funding for the studies included in the review?	**No**	
11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	Yes	
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	Yes	Using meta-regression.
13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?	**No**	No mention in Discussion.

Domain	Response	Reason
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Yes	
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	Yes	
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	**No**	
Overall	***Critically low***	5 critical flaws in domains 2, 4, 11, 13, 16 and a non-critical flaw in domain 9.

2.1 Overall quality

This article is a **critically low** quality review due to 5 critical flaws in domains 2, 4, 11, 13, 16 and a non-critical flaw in domain 9.

3 Risk of bias of the review

3.1 Domain 1: Study eligibility criteria

Subdomain	Response	Reason
1.1 Did the review adhere to pre-defined objectives and eligibility criteria?	**PN**	The study is not pre-registered and the eligibility criteria is not detailed enough showing adherence to a pre-specified protocol. For example, there is no mention of "cavitated" in the eligibility criteria.
1.2 Were the eligibility criteria appropriate for the review question?	Y	The review question is broad so as the eligibility criteria.

Subdomain	Response	Reason
1.3 Were eligibility criteria unambiguous?	Y	The definition for the outcomes of interest is acceptable: "The outcomes of interest were incidence (proportion of individuals developing new carious lesions) and increment (mean of new carious lesions). The increment was reported in any of the following ways: mean of new decayed teeth or surfaces, mean of new decayed and filled teeth, and mean of new decayed, missing, and filled surfaces."
1.4 Were any restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	**N**	Date limitation was not justified well (as discussed in the limitations of the study): "Furthermore, we restricted our search to only studies in English that were published after 1980; comparing the findings of older studies with no fluoride in toothpaste with newer studies could have allowed interpreting the relevance of brushing versus fluoridated toothpaste."
1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)?	**N**	Language limitation was not justified (as discussed in the limitations of the study): "Furthermore, we restricted our search to only studies in English that were published after 1980; comparing the findings of older studies with no fluoride in toothpaste with newer studies could have allowed interpreting the relevance of brushing versus fluoridated toothpaste."
Concerns regarding specification of study eligibility criteria:	***High concern***	Due to unjustified restrictions and lack of a pre-defined protocol.

3.2 Domain 2: Identification and selection of studies

Subdomain	Response	Reason
2.1 Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	Y	PubMed, Embase, CINAHL, and Cochrane Central.

Subdomain	Response	Reason
2.2 Were methods additional to database searching used to identify relevant reports?	**PN**	No mention.
2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?	PY	Appendix Table 1 shows the search strategy used in PubMed. While it could include more keywords, still seems to retrieve eligible studies.
2.4 Were restrictions based on date, publication format, or language appropriate?	**N**	Date, publication format, and language restrictions: "Search filters were used to restrict retrieval to studies in humans, published in English between January 1980 and December 2015, and to journal articles."
2.5 Were efforts made to minimise error in selection of studies?	Y	Screenings done in duplicate: "Screening of titles and abstracts was performed by 2 independent reviewers (S.K. and J.T.)."
Concerns regarding methods used to identify and/or select studies:	***High concern***	Due to language and date restriction and no additional method for citation seeking.

3.3 Domain 3: Data collection and study appraisal

Subdomain	Response	Reason
3.1 Were efforts made to minimise error in data collection?	Y	Data was extracted in duplicate: "Data extraction from the full texts of the articles was independently performed by 2 reviewers (S.K. and J.T.)."
3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	Y	Appendix Table 3 shows the background characteristics and findings from the included studies
3.3 Were all relevant study results collected for use in the synthesis?	Y	"Data on study setting, study design, sample size, follow-up period, dental caries outcome and diagnostic criteria, categories used to record the frequency of toothbrushing, absolute values necessary for meta-analysis, findings, and information on other sources of fluoride were collected."

Subdomain	Response	Reason
3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	Y	Effective Public Health Practice Project (EPHPP) was used for RoB assessment.
3.5 Were efforts made to minimise error in risk of bias assessment?	Y	In duplicate: "Studies were assessed for methodological quality by 2 reviewers (S.K. and J.T.) independently."
Concerns regarding methods used to collect data and appraise studies:	***Low concern***	No serious concern in any subdomain.

3.4 Domain 4: Synthesis and findings

Subdomain	Response	Reason
4.1 Did the synthesis include all studies that it should?	Y	While the data from 8 included studies was not available for meta-analysis, there is no evidence for selective reporting. The authors have also imputed some of the data meaning that it seems they have done their best. Funnel plot is also symmetrical.
4.2 Were all pre-defined analyses reported or departures explained?	NI	
4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	Y	The heterogeneity of the studies was not high and therefore performing meta-analyses was an appropriate decision. Random effect model and meta-regression are also appropriate.
4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	Y	I2 statistics was not high and the possible reasons were also explored by subgroup analyses and meta-regression.
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	Y	Symmetrical funnel plot and non-critical meta-regression coefficient.

Subdomain	Response	Reason
4.6 Were biases in primary studies minimal or addressed in the synthesis?	Y	The majority of the studies had an overall strong or moderate quality. Selection bias in the studies was also minimal.
Concerns regarding the synthesis and findings:	***Low concern***	The findings were so convincing that the only limitation (4.2) would have little impact.

3.5 Overall risk of bias

Summary of concerns in each domain:

Domain	Concern	Reason
1. Concerns regarding specification of study eligibility criteria	***High concern***	Due to unjustified restrictions and lack of a pre-defined protocol.
2. Concerns regarding methods used to identify and/or select studies	***High concern***	Due to language and date restriction and no additional method for citation seeking.
3. Concerns regarding methods used to collect data and appraise studies	***Low concern***	No serious concern in any subdomain.
4. Concerns regarding the synthesis and findings	***Low concern***	The findings were so convincing that the only limitation (4.2) would have little impact.

Risk of bias in the review:

Question	Response	
A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4?	***No***	While the limitation were acknowledged by the authors in discussion, they were not addressed in the interpretation of findings
B. Was the relevance of identified studies to the review's research question appropriately considered?	Yes	

Question	Response	
C. Did the reviewers avoid emphasizing results on the basis of their statistical significance?	Yes	
Risk of bias in the review:	***High***	The phase 2 assessment identified a number of areas of concern with the review process which were not addressed by the authors. These concerns might lead to possibility of missing studies. There is therefore a high risk of bias in this review.