Salivary streptococcus mutans count and caries outcome – a systematic review

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Abstract

OBJECTIVE: To answer whether an increased salivary S. mutans count is associated with higher caries. METHODS: Six databases were searched for articles (4 February 2009). Inclusion criteria: (i) titles/abstracts relevant to topic; (ii) published in English, Portuguese, Spanish; (iii) prospective cohort study; (iv) at least 2 groups/cohorts are investigated, for which a baseline salivary mutans count and a caries outcome after a period of time is reported; (v) caries outcome reported as computable datasets. RESULTS: Fifteen from the initial 134 articles were selected. From these, 5 were rejected and 10 articles reporting on 30 separate datasets accepted. Owing to heterogeneity, no meta-analysis was undertaken. Cohorts which differed statistically significantly ($p<0.05$) in their caries outcomes also differed largely in their salivary SM counts; cohorts with similar ($p>0.05$) caries outcomes differed little. Cohorts with S. mutans count $>10^5$ cfu/ml showed higher caries outcome. The results showed a 55% lower caries risk in subjects with S. mutans $<5 \times 10^5$ cfu/ml (Relative Risk 0.45 - 95% CI 0.34, 0.59 - $p<0.00001$). Potential bias may have influenced study results. CONCLUSION: Increased S. mutans counts are associated with higher caries outcomes. High quality cohort studies are needed to validate the current evidence.

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Introduction

A recent literature search in PubMed, using the terms "dental caries AND etiology", identified more than 12000 articles related to the cause of tooth caries. In these articles, the factors that contribute to caries onset and progression were described. One of the known etiological caries models was proposed by Keys (1960) and describes the interaction of microorganisms, diet and tooth tissue as the main cause for caries development [1]. However, when these factors have been analyzed independently, the isolated role of microorganisms in caries etiology has not been fully understood. Oral colonization by Streptococcus mutans (SM) is required for dental caries initiation and it has been suggested that an SM count higher than 10^5 cfu/ml of saliva is related to higher caries risk [2]. However, some reports have questioned the conclusiveness of salivary SM tests for assessing the risk of future caries [3,4].

Most of the literature produced to answer the question as to whether salivary SM can indeed be related to caries outcome refers to cross-sectional studies. However, the results of cross-sectional studies can only reflect the situation of the studied population at a specific point in time and do not offer opportunities for differentiating between cause and effect [5]. Therefore, any associative relationship between salivary SM and prospective caries risk identified by cross-sectional studies must be interpreted with caution, as these are not able to indicate the sequence of events: e.g. whether the SM exposure occurred before or after the onset of caries [6]. Unlike cross-sectional studies, prospective cohort studies, in which a group of subjects are studied over time, are more suitable for establishing strong associations or even causality inferences between salivary SM and prospective caries risk [5]. In order to apply consistent research results from cohort studies to clinical practice, the latter can be identified through systematic reviews of the literature. Systematic reviews establish where the effects of healthcare are consistent and where they may vary significantly, through the use of explicit systematic review methods that limit bias (also known as systematic error) and reduce the chance of effect [7].

Two published systematic review articles have identified prospective cohort studies regarding the relationship of salivary S. mutans counts and tooth caries [8,9]. The systematic review by Harries et al. (2004) focuses on general risk factors for dental caries, including the salivary S. mutans count, and concludes that an association exists between high levels of Streptococcus mutans in saliva and an increased caries experience [8]. However, the authors derived to their conclusion through narrative synthesis. The disadvantage of narrative synthesis in systematic reviews is that bias may be introduced if the outcomes of some studies are inappropriately stressed over others [10]. This may lead to the error of comparing the number of “positive studies” with the number of “negative studies”. Such “vote counting” is considered unreliable, “since whether a study is counted as ‘positive’ or ‘negative’ may depend on how the results are interpreted by the reviewers and it gives no consideration on the relative weight of reliable evidence contributed by each study [10].

A further tendency is to overlook small but clinically important effects when counting votes, particularly when counting studies with statistically insignificant results as 'negative' or 'inconclusive'.

A second systematic review, by Thenisch et al. (2006), investigated the S. mutans count in plaque and saliva as a predictive factor for caries in pre-school children [9]. In contrast to the Harris et al. (2004) review, this one used quantitative synthesis and attempted meta-analysis where possible. The results showed a pooled risk ratio (RR) of 2.11 with a 95% confidence interval (CI) 1.47 – 3.02, indicating that salivary S. mutans counts appeared to be associated with a considerable increase in caries risk [9]. However, this review was limited to 2-5 year-old children.

The aim of this quantitative systematic review was to answer the question as to whether an increased salivary S. mutans count in patients, without age restriction, is associated with a higher caries outcome.

Materials and methods

Data collection

Five Anglophone databases (Biomed Central; Cochrane Library; Directory of Open Access Journals; PubMed; Science-Direct) and one Lusophone database (Literatura Latino-Americana e Caribenha em Ciências da Saúde – LILACS) were systematically searched, for articles reporting on clinical trials up to the 4th of February 2009. The string of MeSH and text search terms with Boolean operators: *"Dental Caries Susceptibility OR Dental Caries Activity Tests AND Streptococcus mutans AND Colony Count, Microbial"* were used in searching the Anglophone databases and the strings of text terms: "*cárie* AND *mutans*" were used in searching LILACS. In addition, the reference lists of included articles were checked for suitable studies. Articles for review were selected from the search results on the basis of their compliance with the inclusion criteria:

1. Titles/abstracts relevant to topic;
2. Published in English, Portuguese or Spanish;
3. Prospective cohort study design;
4. 2-group analysis should be possible: at least 2 groups/cohorts were investigated, in which a baseline salivary mutans count and a caries outcome (per group/cohort) after a time period is reported; caries outcome data to be reported either as:
   (a) Dichotomous data: number of teeth with caries from total number of teeth reported per group after a period;
   (b) Continuous data: number of evaluated subjects, mean caries outcome with standard deviation or standard error reported per group.

Where only a relevant title without a listed abstract was available, a full copy of the article was assessed for inclusion.

Article review

Only articles that complied with the inclusion criteria were reviewed further. Full copies of articles were reviewed independently by two reviewers (S.M. and S.L.) for compliance with the inclusion criteria. Where several articles had reported on the same study over similar time periods, the article covering the trial most comprehensively in accordance with the inclusion criteria was accepted. Disagreements between reviewers were resolved by discussion and consensus.

Data extraction from accepted trials

The outcome measure was tooth caries measured according to the continuous data values of caries-related indices (i.e. DMFS/dmfs) or the index increment, as well as the dichotomous number of carious teeth versus caries-free teeth at the end of the study period. Individual datasets, including number of evaluated subjects, mean and standard deviation (SD) for continuous data, number of carious teeth (n) and total number of evaluated teeth (N) for dichotomous datasets were extracted from the accepted articles. Where possible, missing data were calculated from information given in the text or tables. In addition, authors of articles were contacted in order to obtain missing information. Disagreements between reviewers during data extraction were resolved through discussion and consensus.

Quality of studies

The quality assessment of the accepted trials was undertaken independently by two reviewers (SM and SL) following STROBE-based guidelines [11]. Trials not included in this review were used to pilot the process. A quality assessment rating scored by both reviewers was subsequently derived by consensus. The following quality criteria were examined:

(1) Matching of cohorts:
(A) adequate - clear statement in text that cohorts were matched;
(B) unclear - unclear or no statement in text that cohorts were matched;
(C) inadequate – baseline data differed significantly between cohorts ($p<0.05$).

(2) Representativeness of cohorts for their population:
(A) adequate – clear statement in text that subjects were randomly selected;
(B) unclear – unclear, or no statement in text, that subjects were randomly selected;
(C) inadequate - clear statement in text about selection procedure indicating a non-random selection.

(3) Confounder assessment:
(A) adequate - confounders accounted for and statistically adjusted;
(B) unclear – confounders not accounted for;
(C) inadequate – confounders accounted for but not statistically adjusted.

(4) Blind/masked outcome assessment recorded:
(A) yes;
(B) not clearly recorded;
(C) no;
(D) not possible

(5) Were all cohorts measured in the same way?
(A) adequate – it is clear from the text that cohorts were measured in the same way;
(B) unclear – it is not clear from the text that cohorts were measured in the same way;

(C) inadequate – it is clear from the text that cohorts were not measured in the same way.

Statistical Analysis

A random effects model in RevMan Version 4.2 statistical software (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2003) was used. Differences in treatment groups were computed on the basis of Mean Differences (MD), with 95% confidence intervals (CI) for continuous datasets and Relative Risk (RR) with 95% confidence intervals (CI) for dichotomous datasets. Datasets were assessed for their clinical and methodological heterogeneity, following Cochrane guidelines [12]. Datasets were considered to be heterogeneous if they did differ in caries outcome measure, age of patients, identified cut-off points for salivary S. mutans counts, length of follow-up period and type of reported data. Chi^2, degree of freedom (df) and the percentage of total variations across datasets (I^2) were used in assessing statistical heterogeneity [13]. Only identified homogeneous datasets were considered fit for pooling by meta-analysis. Pooled datasets were assigned a Mantel-Haenszel weight directly proportional to their sample size.

Results

An initial search of PubMed resulted in 134 articles, of which 14 [3,4,14-25] were selected in compliance with the inclusion criteria. A subsequent search of the other four Anglophone databases generated no further results. The search in LILACS resulted in 37 articles, of which one [26] was accepted. After further review, five articles [14,15,19,20,25] were excluded from the 15 initially selected cohort studies, owing to lack of reported computable data specified by the inclusion criteria of this review. Table 1 provides information about quality aspects assessed for the 10 accepted cohort studies. The matching of cohorts was rated A (adequate) for 2 studies [17,24] and 1 study [4] was rated adequate for its representiveness, while 2 [3,24] reported that their cohort selection was non-random. Most studies did not report on important confounders (Table 2). Only one accounted for and corrected confounders [3], while 6 [16,18,21-24] accounted for them without correcting the confounder impact statistically. The study by Fure (1998) reported a statistically significant difference ($p<0.05$) in number of remaining teeth and salivary S. sobrinus count between the cohorts at baseline [23], while Thibodeau and O'Sullivan (1995) reported a statistical difference ($p<0.05$) in the baseline dmfs between cohorts [18].

From the 10 accepted articles, 27 separate computable continuous and 3 dichotomous datasets with relevance to the review question were extracted. The main characteristics of the datasets are described in Table 3. It has to be noted that 3 of the accepted articles reported on different datasets from the same study [18,21,22]. Clinical and methodological heterogeneity between all datasets was observed. The datasets differed in caries outcome measure, age of patients, identified salivary S. mutans counts per cohort, length of follow-up period and type of reported data. For that reason, no meta-analysis was conducted and statistical heterogeneity was not further assessed. Instead the mean difference (MD) and relative risk (*RR*) with 95% confidence interval (CI) were calculated for the datasets separately and the differences between cohorts per dataset tested for statistical significance (Table 4). The results showed that cohorts, which differed statistically significantly ($p<0.05$) in their caries outcomes also differed largely in their salivary SM counts, while cohorts with similar ($p>0.05$) caries outcomes differed little (Table 3 and 4). Cohorts with a salivary S. mutans count above 10^5 cfu/ml showed a higher caries outcome than cohorts with salivary S. mutans count below 10^5 cfu/ml [3,4]. The study by Petti and Hausen (2000) reported a relative risk of 0.45 (95% CI 0.34, 0.59 – $p<0.00001$), which indicates that cohorts with a salivary S. mutans count less than 5×10^5 cfu/ml will experience 55% less caries incidence than cohorts with a salivary S. mutans count above 5×10^5 cfu/ml [3].

Discussion

Quantitative systematic reviews with meta-analysis enable the collating of clinical information from separate studies carried out for a specific clinical observation, in comparison to others, and allow detection of statistically significant ($p<0.05$) differences [10]. In that way a more objective assessment of the currently available evidence is possible. In this case, the clinical caries outcome between different salivary SM counts at baseline was compared. However, due to aspects of clinical and methodological heterogeneity of included studies, the outcome data were not directly comparable. Therefore meta-analysis of the quantified study results was not possible. Other aspects of this review may also have contributed to limitations in its results: (i) not all relevant publications were listed in the selected databases; (ii) not all relevant publications were published in English, Portuguese or Spanish; (iii) the chosen strings of search terms may not have been broad enough to have captured all articles listed in the databases. Thus, some relevant studies may not have been identified.

This was the first quantitative systematic review regarding the relation of salivary SM counts to caries outcome not limited to subjects aged <5 years. The results show that individuals with a higher salivary S. mutans count presented a higher caries outcome than those with a lower salivary S. mutans count (Tables 3 and 4). The results also indicate that the presence of salivary SM is associated with high dmfs/DMFS scores in children and this is in line with previous systematic review results for children aged <5 years [9]. However, for adults the same could not be established, since only one article that had investigated a cohort of elderly subjects (age >60 years) was found [23].

This review also identified reports on limitations of salivary SM for caries risk assessment. Fure (1998) observed that age was the best predictor for caries incidence in elderly people, although salivary conditions also impacted upon their overall oral heath status [23]. Miró et al. (1989) investigated two different cohorts of children (2 to 3 and 6 to 12 year-olds, respectively) for a period of 1 year and concluded that the salivary S. mutans predictive values alone were not sufficient determiners of caries activity [26]. In this circumstance other parameters, such as past caries experience and educational levels of parents, needed to be analysed in order to reach validity in caries prognosis. The study by Twetman et al. (1994) stated that clinical examination of past caries experience may be useful in the assessment of caries risk for children and, therefore, in the planning of preventive measures [17]. According to Petti and Haussen (2000) the established salivary S. mutans counts provide considerable information only on children with bad

oral health hygiene and low fluoride exposure [3]. However, these children are already known to be at high caries risk. For that reason, the potential confounders for dental caries, such as fluoride exposure, oral hygiene, dietary factors, saliva flow rate and socio-economic status, should be taken into account. Another aspect that makes the comparison of the results from different studies difficult refers to the methodology used. Sample selection, bacterial dental plaque or saliva and the medium employed for mutans analysis also affect the overall outcomes [27,28]. In addition, a higher predictive value for plaque SM counts rather than saliva samples indicates that sampling for saliva, although easier to do, may limit the accuracy of caries risk assessment [24]. A group of cariogenic bacteria commonly cultured from the mouth of young children comprises Streptococci (mutans and sobrinus) [24]. Rupf et al. (2006) compared caries activity in S. mutans positive children with that in children infected with both S. mutans and S. sobrinus [4]. The results showed a significant increase of DMFS in children harbouring both S. mutans and sobrinus. Other studies reported a similar outcome, in that children harbouring both S. mutans and sobrinus had significantly higher caries prevalence than those with either S. mutans or S. sobrinus, only [30,31].

Despite these limitations, this review identified a statistically higher caries outcome in all cohorts with a higher salivary S. mutans count (Table 3 and 4). The continuous datasets #03 and 04; #08; #26 from the studies by Rupf et al. (2006); Fure (1998) and Thibodeau and O'Sullivan (1996), respectively, all show statistically highly significant ($p<0.00001$) mean differences (MD) in caries outcomes between their compared cohorts [4,22,23]. Cohorts from these studies with increased caries outcomes had mean salivary SM counts of permanently over 10^5 cfu/ml [4], 9.8 x 10^5 cfu/ml [23] and >50 cfu [22] as compared to <10^5 cfu/ml [4], 4.6 x 10^5 cfu/ml [23] and 0 cfu [22], respectively. The dichotomous results presented by Petti and Hausen (2000) also show a statistically highly significant ($p<0.00001$) higher number of carious teeth for subjects with salivary SM counts above 5 x 10^5 cfu/ml than for subjects below 5 x 10^5 cfu/ml after 2 years [3]. The findings of this study, together with the results from the cohort studies by Rupf et al. (2006) and Fure (1998), confirm an association of higher caries outcomes with S. mutans counts above 10^5 cfu/ml in saliva [4,22,23]. In contrast, no statistically significant higher caries outcomes were observed for cohorts with low salivary SM (datasets #10,19,22,29,30) [18,22,26]. Moreover, the lack of large differences in salivary SM between compared cohorts (datasets #01,05,07,09 [4,23,24]; #13,16,18,24 [17,22]) was identified as further reason for lack of statistical significance in caries outcomes.

The results of this quantitative systematic review, that individuals with a higher salivary S. mutans count presented a higher caries outcome than those with lover salivary S. mutans count, are in line with previous systematic review [8,9]. However, these results need to be regarded with caution as bias may have influenced the outcome of most of the identified cohort studies (Table 1). Only 2 studies provided a clear description on the matching process for cohort subjects [17,24]. Information from all other studies was considered unclear on this point. A potential lack of sufficient similarity between cohorts due to lack of matching may introduce a selection bias: one cohort may have been more susceptible to caries than the other from the onset. Furthermore, because of the lack of confounder reporting (Table 2) it is unclear whether the included cohorts were exposed to a performance bias, i.e. through fluoride exposure or increased oral hygiene measures, throughout the studies. Additionally, detection bias may also have been possible, since it remains unclear whether the evaluators knew about the baseline salivary S. mutans count of cohorts when assessing the caries outcome. Such bias or systematic error may affect studies by causing either over- or under-estimation of the observed outcome effect. Overestimation of such effect has been observed to be the most common [32]. Schulz et al. (1995) reported a 41% treatment effect overestimation solely due to selection bias [33]. For these reasons further high quality cohort studies are needed in order to validate the current evidence for an association of salivary S. mutans with higher caries outcome over time. It is recommended that reporting of such progressive cohort studies should follow the STROBE statement [11] and, particularly, include a clear description of the sources and methods of participant selection, including eligibility criteria; clear definition of all outcomes, exposures, potential confounders and effect modifiers; a description of matching criteria; as well as a description of statistical methods used to control confounding.

Conclusion

This quantitative systematic review confirms the association between increased salivary S. mutans count (>10^5 cfu/ml) with higher caries outcome over time. However, owing to the potential influence of systematic error/bias on the results of most of the reviewed studies, it is recommended that further high quality cohort studies be undertaken in order to validate the currently available evidence.

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Table 1. Quality assessment of cohort studies

Article	Selection bias		Performance bias	Detection bias	
	Groups are matched	Representative-ness of groups	Confounders accounted for	Evaluator blinding	Both groups measured the same way
Rupf et al., 2006 [4]	B	A	B	B	A
Sanchéz-Pérez and Acosta-Gío, 2001 [24]	A	C	C	B	A
Fujiwara et al., 1991 [16]	B	B	C	B	A
Fure, 1998 [23]	B	B	C	B	A
Thibodeau and O'Sullivan, 1995 [18]	B	B	C	B	A
Twetman et al., 1994 [17]	A	B	B	B	A
O'Sullivan and Thibodeau, 1996 [21]	B	B	C	B	A
Thibodeau and O'Sullivan, 1996 [22]	B	B	C	B	A
Petti and Hausen, 2000 [3]	B	C	A	B	A
Miró et al., 1989 [26]	B	B	B	B	A

Table 2. Potential confounders with influence on caries outcome reported

Article	Confounder					
	Fluoride exposure	Oral hygiene measures	Saliva function	Caries activity (at baseline)	Salivary S. sobrinus count per cohort	Carbohydrate diet
Rupf et al., 2006 [4]	Not reported	Not reported	Not reported	Not reported	Both groups S. sobrinus negative	No reported
Sanchéz-Pérez and Acosta-Gío, 2001 [24]	All participants from non-fluoridated area (water fluoride content 0.02 parts x 10^6 F)	Not reported	No xerostomia in both groups	Low SMS group = caries free; High SMS group = >4 dmfs at baseline	Not reported	Not reported
Fujiwara et al., 1991 [16]	Non-fluoridated water supply	Not reported	Not reported	Caries free	Not reported	Not reported
Fure, 1998 [23]	Not reported	DS PS% (baseline) MD p 06 -3.50 0.57 07 -14.80 0.10 08 -11.30 0.24	DS Buffer final pH (baseline) MD p 06 0.50 0.19 07 0.70 0.09 08 0.20 0.65	DS NRT MD p 06 4.50 0.0004 07 7.70 0.0007 08 3.20 0.19	DS $X10^5$ cfu (baseline) MD p 06 -1.50 0.003 07 -2.70 0.06 08 -1.20 0.43	Not reported
Thibodeau and O'Sullivan, 1995 # [18]	Not reported	Not reported	Not reported	DS dmfs (baseline) MD p 09 -1.29 0.01 10 -3.21 0.0007 11 -1.92 0.03	Not reported	Not reported
Twetman et al., 1994 [17]	Not reported	Not reported	Not reported	DS dmfs (baseline) MD p 12-17 -0.10 0.77	Not reported	Not reported
O'Sullivan and Thibodeau, 1996 # [21]	Exposure to 'optimally' fluoridated water	Not reported	Not reported	Caries free	Not reported	Not reported
				Caries-positive		
Thibodeau and O'Sullivan, 1996 # [22]				Caries-positive		
Petti and Hausen, 2000 [3]	Not reported	Not reported	Not reported	All participants caries free	Not reported	Not reported
Miró et al., 1989 [26]	Not reported	Not reported	Not reported	No reported	Not reported	Not reported

DS = Dataset number; PS% = Percentage of tooth surfaces harboring plaque; MD = Mean difference; p = P-value; NRT = Number of remaining teeth. # Articles reporting on different datasets from the same studies

Table 3. Characteristics of datasets with potential influence on study outcome

Author	DS	Caries outcome measure	Patient age/gender	SM measuring		SM measurements at baseline		Follow-up period	Type of data reported
				Saliva type	Point of measurement	Cohort with lower SM	Cohort with higher SM		
Rupf et al., 2006 [4]	01	Caries increment $D_{1,2}$ DMFS	7-12 years	Stimulated saliva	Throughout study period	$10^{3-<5}$ cfu/ml	Temporary high at $10^{>5}$ cfu/ml	4 years	Continuous
	02	Caries increment $D_{3,4}$ DMFS							
	03	Caries increment $D_{1,2}$ DMFS					Permanently high at $10^{>5}$ cfu/ml		
	04	Caries increment $D_{3,4}$ DMFS							
Sanchéz-Pérez and Acosta-Gío, 2001 [24]	05	dmfs /DMFS	8-10 years 30 boys and 30 girls	Stimulated saliva Dental plaque - hypodermic needle	At baseline	Initial $\log_{10}$ counts (mean) = 1.4 (SD 0.97)	Initial $\log_{10}$ counts (mean) = 2.1 (SD 0.45)	18 months	
Fujiwara et al., 1991 [16]	06	def index	0-2 years	Unstimulated saliva	At baseline	<10 cfu	>10 cfu	12 months	
Fure, 1998 [23]	07	DFS% increment	60 versus 70 year olds	Unstimulated saliva	At baseline and end of study	4.6 (SD 7.4) x10^5 cfu/ml	8.0 (SD 13.9) x10^5 cfu/ml	5 years	
	08		60 versus 80 year olds			4.6 (SD 7.4) x10^5 cfu/ml	9.8 (SD 24.6) x10^5 cfu/ml		
	09		70 versus 80 year olds			8.0 (SD 13.9) x10^5 cfu/ml	9.8 (SD 24.6) x10^5 cfu/ml		
Thibodeau and O'Sullivan, 1995# [18]	10	dmfs increment	3.8 years	Unstimulated saliva	At baseline	0	1-50 cfu	6 years	
	11					0	>50 cfu		
	12					1-50 cfu	>50 cfu		
Twetman et al., 1994 [17]	13	dmfs increment	4 years	Stimulated saliva	At baseline	0-4 cfu	5-29 cfu	2 years	
	14					0-4 cfu	30-199 cfu		
	15					0-4 cfu	>200 cfu		
	16					5-29 cfu	30-199 cfu		
	17					5-29 cfu	>200 cfu		
	18					30-199 cfu	>200 cfu		
O'Sullivan and Thibodeau, 1996# [21]	19	dmfs increment	3.8 years	Unstimulated saliva		0	1-50 cfu	2 years	
	20					0	>50 cfu		
	21					1-50 cfu	>50 cfu		

	22					0	1-50 cfu		
	23					0	>50 cfu		
	24					1 – 50 cfu	>50 cfu		
Thibodeau and O'Sullivan, 1996# [22]	25	dmfs	3.8 years	Unstimulated saliva		0	1-50 cfu	2 years	
	26					0	>50 cfu		
	27					1-50 cfu	>50 cfu		
Petti and Hausen, 2000 [3]	28	Number of carious teeth	6-7 years	Unstimulated saliva	Throughout study period (every 3 months)	<5 x 10^5 cfu/ml	>5 x 10^5 cfu/ml	2 years	Dichotomous
Miró et al., 1989 [26]	29	Number of carious teeth	2-3 years	No information whether stimulated or unstimulated	At baseline	0	>10 cfu	12 months	
	30		6-12 years						

DS = Dataset number; SM = S. mutants salivary count; SD = Standard deviation; cfu = Colony forming units; def = index (decayed primary teeth for filling, - for extraction, filled primary teeth).
# Articles reporting on different datasets from the same studies

Table 4. Comparison of caries outcome between cohorts with low and high salivary S.mutans count at baseline per dataset

				Continuous data
Article	DS	MD	95%CI	p– value
Rupf et al., 2006 [4]	01	-3.30	-7.12, 0.52	0.09
	02	-4.30	-8.03, -0.57	0.02*
	03	-5.60	-7.61, -3.59	<0.00001*
	04	-8.60	-12.26, -4.94	<0.00001*
Sanchéz-Pérez and Acosta-Gío, 2001 [24]	05	-1.10	-3.28, 1.08	0.32
Fujiwara et al., 1991 [16]	06	-5.31	-8.00, -2.62	0.0001*
Fure, 1998 [23]	07	-4.50	-9.29, 0.29	0.07
	08	-10.60	-15.48, -5.72	<0.00001*
	09	-6.10	-12.53, 0.33	0.06
Thibodeau and O'Sullivan, 1995# [18]	10	-1.92	-5.03, 1.19	0.23
	11	-8.36	-13.86, -3.40	0.001*
	12	-6.71	-12.54, -0.88	0.02*
Twetman et al., 1994 [17]	13	-0.20	-0.99, 0.59	0.62
	14	-1.10	-1.77, -0.43	0.001*
	15	-2.30	-3.35, -1.25	0.0001*
	16	-0.90	-1.83, 0.03	0.06
	17	-2.10	-3.32, -0.88	0.0008*
	18	-1.20	-2.35, -0.05	0.04*
O'Sullivan and Thibodeau, 1996# [21]	19	0.05	-0.97, 1.07	0.92
	20	-3.50	-6.17, -0.83	0.01*
	21	-3.55	-6.12, -0.98	0.001*
	22	-2.28	-5.51, 0.95	0.17
	23	-3.50	-6.45, -0.55	0.02*
	24	-1.22	-4.41, 1.97	0.45
Thibodeau and O'Sullivan, 1996# [22]	25	-3.35	-5.74, -0.96	0.006*
	26	-5.98	-8.56, -3.40	<0.00001*
	27	-2.63	-5.76, 0.50	0.10
				Dichotomous data
Article	DS	*RR*	95%CI	*p*– value
Petti and Hausen, 2000 [3]	28	0.45	0.34, 0.59	<0.00001*
Miró et al., 1989 [26]	29	1.41	0.49, 4.01	0.52
	30	0.49	0.04, 5.46	0.57

DS = Dataset number; MD = Mean differences; RR = Relative risk; CI = Confidence interval.

* Datasets reporting a significantly higher caries outcome for cohorts with higher salivary S. mutans count at baseline # Articles reporting on different datasets from the same studies.