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Caries Prevalence in Non-Syndromic Patients with Cleft Lip and/or Palate: A Meta-Analysis

ANTONARAKIS, G S, PALASKA, P-K, HERZOG, Georges

Abstract

Aim: To evaluate caries prevalence in non-syndromic patients with cleft lip and/or palate (CLP) in comparison with a matched non-CLP population. Methods: A literature search was conducted in order to identify articles reporting on the prevalence of caries in CLP versus non-CLP individuals. The related citations function in PubMed and reference lists of retrieved articles were used to expand the search. Only studies with a suitable matched control group were included. From each included study, study and sample characteristics were extracted, as were results. The main outcome was the score given for caries prevalence in each study, using a well-defined index. The data were entered into meta-analysis software and a meta-analysis performed using the random-effects model. Results: From the 592 articles initially identified, 7 were chosen according to preset inclusion and exclusion criteria. All of the studies were cross-sectional in nature, and used the decayed, missing, and filled (DMF/dmf) indices as the final outcomes. The included studies involved a total of 474 CLP patients aged 1.5-29 years. When looking at permanent [...]

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Caries Prevalence in Non-Syndromic Patients with Cleft Lip and/or Palate: A Meta-Analysis

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Key Words
Caries prevalence · Cleft lip and/or palate · Meta-analysis

Abstract
Aim: To evaluate caries prevalence in non-syndromic patients with cleft lip and/or palate (CLP) in comparison with a matched non-CLP population. ***Methods:*** A literature search was conducted in order to identify articles reporting on the prevalence of caries in CLP versus non-CLP individuals. The related citations function in PubMed and reference lists of retrieved articles were used to expand the search. Only studies with a suitable matched control group were included. From each included study, study and sample characteristics were extracted, as were results. The main outcome was the score given for caries prevalence in each study, using a well-defined index. The data were entered into meta-analysis software and a meta-analysis performed using the random-effects model. ***Results:*** From the 592 articles initially identified, 7 were chosen according to preset inclusion and exclusion criteria. All of the studies were cross-sectional in nature, and used the decayed, missing, and filled (DMF/dmf) indices as the final outcomes. The included studies involved a total of 474 CLP patients aged 1.5–29 years. When looking at permanent teeth, data from 5 studies suggest that CLP patients have a higher number of DMF teeth than the controls (mean difference 1.38; p = 0.003). For deciduous teeth, data from 4 studies suggest that CLP patients have a higher number of dmf teeth than the controls (mean difference 1.51; p = 0.03). ***Conclusion:*** Non-syndromic patients with CLP tend to have higher caries prevalence, both in the permanent and the deciduous dentition, in comparison with matched non-CLP controls.

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According to a recent Centers for Disease Control and Prevention [CDC, 2006] report, cleft lip and/or palate (CLP) is the second most common birth defect, occurring in 1 in 575 live births. Children born with CLP may be affected by a combination of various facial differences, disturbances of the dentition and growth of the jaws, as well as swallowing, speech, and hearing disorders [Klassen et al., 2012]. A healthy dentition is of principal importance for reasons such as the desire to preserve bone, and to maintain a satisfactory occlusion. Dental caries is one of the most common preventable diseases [Selwitz et al., 2007] and their prevention and early detection should thus be an important aspect of the multidisciplinary management of CLP patients.

One of the earliest studies performed on the dentition of CLP children found that caries experience of these children did not differ markedly from that of normal children [Lauterstein and Mendelsohn, 1964]. Many studies have been carried out since, looking into caries in CLP patients,

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with contradictory results. Some studies find no difference in caries prevalence between CLP and control patients, while other studies find an increased prevalence in CLP patients [Hasslöf and Twetman, 2007]. The inconsistencies found in different studies can be due to a multitude of reasons such as the multifactorial nature of dental caries, methodological differences, small sample sizes, large age ranges, patients' dental awareness, and cultural differences [Cheng et al., 2007; Hasslöf and Twetman, 2007].

Previous attempts at reviewing the subject of caries prevalence in CLP patients have led to tendencies being detected in the literature, but without quantification. In a review of oral health of CLP patients by Wong and King [1998], the authors state that epidemiological data on caries in CLP children suffer from methodological deficiencies. They further state that their review shows that there is some evidence that CLP children may have a higher caries prevalence than normal children, especially in the primary dentition. Hasslöf and Twetman [2007] in their systematic review on caries in CLP patients found a tendency for more caries in the primary dentition among children with CLP, but no firm conclusion could be made based on their evaluation.

To the best of our knowledge, no previous attempt has been made to use meta-analysis methodology for the purposes of quantifying the difference in prevalence of caries between a CLP and a non-CLP population. The purpose of the present investigation was thus to evaluate caries prevalence in non-syndromic patient populations with CLP, in comparison with matched non-CLP populations.

Methods

Protocol and Registration

When planning and carrying out the present meta-analysis, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed as best as possible [Liberati et al., 2009]. Methods of analysis, inclusion and exclusion criteria, and the main outcome measure were defined in advance of the study. A review protocol was not published and the study was not registered.

Eligibility Criteria

Studies evaluating caries prevalence in non-syndromic CLP patients were investigated. Trials were retrieved with no date, language, or publication status restriction. The method under evaluation was the use of a caries experience index to evaluate caries prevalence.

Inclusion criteria were: (1) cross-sectional or longitudinal studies evaluating caries prevalence in CLP patients at least at one time point; (2) the presence of a suitable matched control group (healthy non-CLP individuals); (3) the use of an index with defined criteria measuring caries experience (caries prevalence); (4) the presentation of results of CLP patients and non-CLP patients presented separately.

Exclusion criteria were: (1) case reports or case series (sample size ≤10); (2) lack of a suitable matched control group; (3) CLP and control group samples of different sizes; (4) literature reviews; (5) commentaries, editorials, or author's replies; (6) the inclusion of syndromic CLP patients; (7) the inclusion of other craniofacial anomalies or dentofacial deformities; (8) the use of outcome measures other than caries prevalence/caries experience; (9) intervention studies; (10) insufficient statistical data for inclusion in a meta-analysis.

The main outcome was caries prevalence in CLP patients at any given time point (no limitation regarding the age of the subjects was imposed), in comparison with a matched non-CLP control group.

Information Sources and Search

Relevant studies were located by searching the following databases: PubMed, EMBASE, Scopus, Web of Science, CINAHL, and the Cochrane Library. The 'related citations' function in PubMed was used to retrieve further articles. The reference lists of the retrieved articles were hand-searched to identify studies that might not have been included. The last search was conducted in October 2012.

The search and study selection were carried out independently by two reviewers. The keywords used in the search strategy were the following: (1) cleft; (2) caries, dental caries, decay, tooth decay. Searches were conducted using a combination of the keyword from the first search category with one of the keywords from the second search category.

Study Selection

Titles and abstracts of the articles were initially evaluated. Full-text articles were retrieved from the potentially eligible studies. If eligibility could not be determined based on the title or abstract, its full text was retrieved. Full-text articles were retrieved and assessed for eligibility by applying the inclusion and exclusion criteria. Finally, eligible studies were collected for data extraction. If the two reviewers could not agree on the eligibility of a certain study, disagreements were resolved by discussion.

Data Collection Process and Data Items

From each included study the following information was extracted: publication data (journal, title, authors, authors' affiliations, date), study design, CLP sample characteristics (sample size, ethnicity, gender, age, types and distribution of CLP), control sample characteristics (type of matching, sample size, ethnicity, gender, age), outcome (the caries prevalence index used and diagnostic criteria used, the exact outcome measures, the way the caries examination was carried out), the presence of some form of error of the method assessment, caries prevalence results (data) presented. Risk of bias within individual studies was assessed by considering the method of matching, and the exact way that the caries examination was carried out. Disagreements were resolved by discussion between the reviewers.

Quality assessment was carried out by evaluation of the included studies in order to determine the degree to which they fulfilled the items on the checklist of aspects of methods to be included in reports assessing caries experience, proposed by Agbaje et al. [2012].

Summary Measures and Synthesis of Results

The difference in means was the main summary measure, comparing the CLP sample to the non-CLP matched control sample. The data were entered into the meta-analysis software of the Co-

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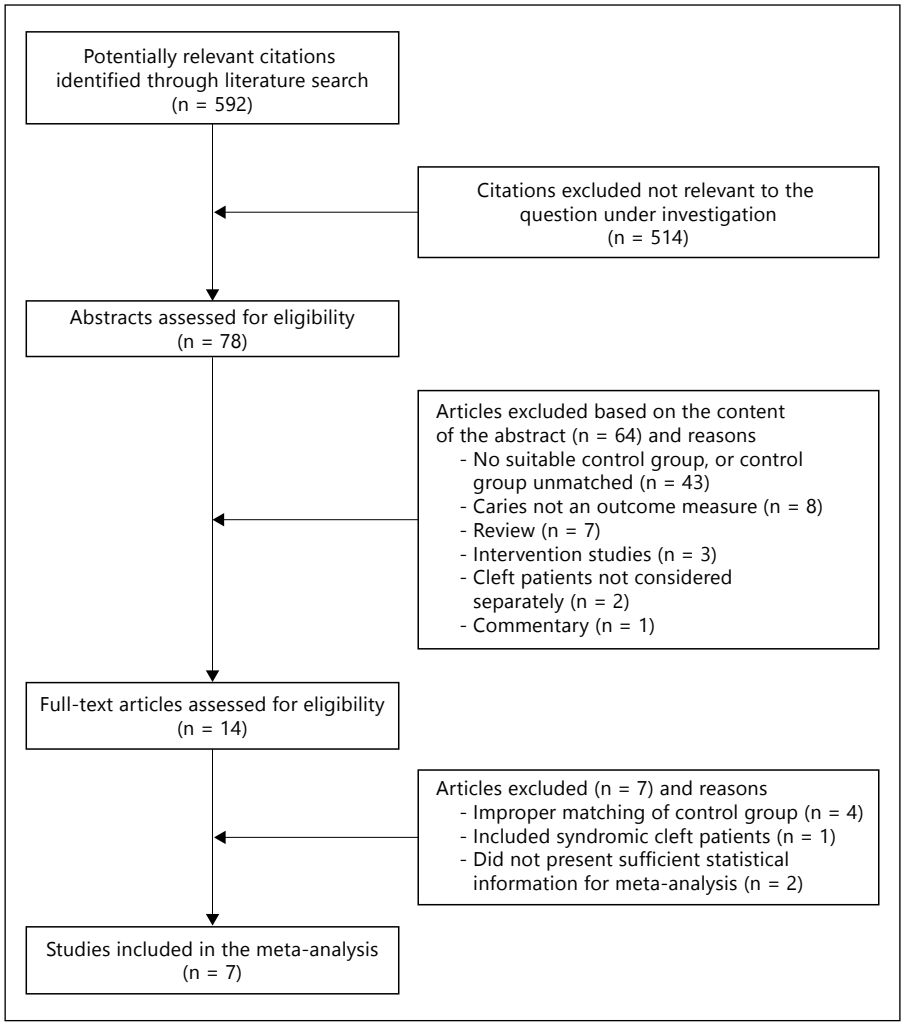

Fig. 1. Flow diagram summarizing the literature search/strategy.

chrane Collaboration (RevMan 5.1, released 22 March 2011). The meta-analyses were performed using the random-effects model of meta-analysis, obtaining mean differences and 95% confidence intervals of the main outcome. Forest plots were drawn and significance tests carried out (calculating p values).

Heterogeneity tests were carried out using various methods, both visual and statistical. Visually, if confidence intervals for the results of individual studies (depicted graphically using horizontal lines) have poor overlap, this generally indicates the presence of statistical heterogeneity. More formally, statistical tests for heterogeneity were used, namely χ^2 tests, Tau^2, as well as calculation of I^2. The χ^2 assesses whether observed differences in results are compatible with chance alone. A low p value (or a large χ^2 statistic relative to its degree of freedom) provides evidence of heterogeneity of treatment effects (variation in effect estimates beyond chance). Tau^2 measures the between-study variance for random-effects meta-analyses. I^2 measures the percentage of total variation across studies due to heterogeneity. A value greater than 50% may be considered substantial heterogeneity.

The risk of bias across studies was carried out by visual inspection of funnel plots. No additional analyses were carried out.

Results

Study Selection

The initial database search yielded 592 articles. After preliminary exclusion, 78 articles remained and were screened for eligibility. Following exclusion on the basis of the content of the abstract, 14 articles were evaluated in their full-text form. Strict application of the inclusion and exclusion criteria provided 7 studies [Lucas et al., 2000; Al-Wahadni et al., 2005; Mutarai et al., 2008; Al-Dajani, 2009; Hazza'a et al., 2011; Freitas et al., 2012; King et al., 2012] that were included in the present meta-analysis (fig. 1).

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Study Characteristics

The characteristics of the included studies are presented in table 1. All of the studies were cross-sectional in nature, and used the decayed, missing, and filled teeth and/or surfaces in the deciduous teeth (dmft/dmfs) index and/or the permanent dentitions (DMFT/DMFS) index as the final outcomes [WHO, 1987, 1997]. The included studies involved a total of 474 CLP patients and 474 matched control patients. The age range of the combined sample was 1.5–29 years. The reporting of information in individual studies was not always complete. For example, one study [Al-Dajani, 2009] did not report on the exact types of CLP of the patient sample, the number of examiners, or error of the method measurements, while another study [Freitas et al., 2012] did not report on the specific caries diagnostic criteria used.

In terms of the quality assessment (table 2) using the checklist proposed by Agbaje et al. [2012], if the number of fulfilled items on the checklist can be arbitrarily divided into 0–4 (poor quality), 5–8 (medium quality), and 9–12 (good quality), then 4 of the studies were of good quality, 2 of medium, and 1 of poor quality.

Results of Individual Studies, Bias, and Synthesis of Results

Within-study bias was present mostly in 2 of the studies as regards matching or caries assessment. Al-Dajani [2009] did not report on the number of examiners carrying out the caries assessment, or error of the method measurements. In this study, the control sample was matched for sex but not formally for age, since sex-matched siblings were used. Mutarai et al. [2008] matched their control sample for age and for other factors, but not formally for sex, meaning that the sex distribution in the CLP versus the control sample was not identical.

The outcomes for permanent teeth (DMFT and DMFS) and those for deciduous teeth (dmft and dmfs) were looked at separately (fig. 2). When looking at permanent teeth, data from 5 studies with a total sample size of 273 suggest that CLP patients have a higher DMFT than the control, with a mean difference of 1.38 (p = 0.003). When looking at DT, MT, and FT separately, data from 2 studies with a total sample size of 62 show that only FT showed a statistically significant difference between the two groups whereby CLP patients have a higher FT than control patients, with a mean difference of 0.91 (p = 0.02). No statistically significant differences were noted when looking at DMFS, based on a total of 90 patients from 2 studies.

Table 1. Characteristics of included studies

Authors and year:	Al-Dajani [2009]	Al-Wahadni et al. [2005]	Freitas et al. [2012]	Hazza'a et al. [2011]	King et al. [2012]	Lucas et al. [2000]	Mutarai et al. [2008]
Country	Syria	Jordan	Brazil	Jordan	Hong Kong	UK	Thailand
Age	12–29 years	10–15 years (n = 13) 16–28 years (n = 19)	12–21 years	4–8 years (n = 36) 8–12 years (n = 24) 12–23 years (n = 38)	2–4 years (n = 71), 5–7 years (n = 61)	3–15 years	1.5–3 years
Sample size	53 cleft, 53 control	32 cleft, 32 control	30 cleft, 30 control	98 cleft, 98 control	132 cleft, 132 control	60 cleft, 60 control	69 cleft, 69 control
Study design	cross-sectional	cross-sectional	cross-sectional	cross-sectional	cross-sectional	cross-sectional	cross-sectional
Type of clefts	not specified	UCLP or BCLP	CLP (n = 13), CL (n = 11), CP (n = 6)	UCLP (n = 52) BCLP (n = 46)	UCLP (n = 80), BCLP (n = 27), CP (n = 25)	UCLP	UCLP (n = 30), BCLP (n = 14), CL (n = 11), CP (n = 14)
Matching	sex-matched siblings	sex, age	sex, age, living habits, orthodontic devices	sex, age	sex, age, ethnicity, socioeconomic status	sex, age, ethnicity, social class	age, domicile, caregiver's education
What looked at	DMFT	DT, MT, FT, DMFT	DT, MT, FT, DMFT, DS, MS, FS, MDFS	dmft, DMFT	dt, mt, ft, dmft	dmft, dmfs, DMFT, DMFS	dmft
How looked at	clinical	clinical	clinical	clinical	clinical	clinical	clinical
Examiners	not specified	1 examiner	1 examiner	1 examiner	1 examiner	1 examiner	1 examiner
Diagnostic criteria	WHO [1987]	WHO [1987]	unspecified	WHO [1997]	WHO [1997]	WHO [1987]	WHO [1997]
Error of method	no	intra-examiner reliability	intra-examiner reliability	intra-examiner reliability	intra-examiner reliability	intra-examiner reliability	intra-examiner reliability

BCLP = Bilateral cleft lip and palate; CL = cleft lip; CP = cleft palate; n = sample size; UCLP = unilateral cleft lip and palate.

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Table 2. Checklist of aspects to be included in reports of surveys assessing caries experience

Item	Survey method	Al-Dajani [2009]	Al-Wahadni et al. [2005]	Freitas et al. [2012]	Hazza'a et al. [2011]	King et al. [2012]	Lucas et al. [2000]	Mutarai et al. [2008]
1	Standardization criteria used	X	X		X	X	X	X
	Materials and settings							
2	Probe type and usage	X	X	X	X	X		X
3	Light conditions			X	X			X
4	Radiographs	X	X	X	X	X	X	X
5	Cleaning	X		X	X	X	X	X
	Detection threshold							
6	Level of lesion detection				X	X		
	Examiner characteristics							
7	Examiner recruitment					X		X
8	Number of examiners involved		X	X	X	X	X	X
9	Examiner training			X		X		X
	Validation							
10	Calibration			X			X	X
11	Reliability testing		X	X	X	X	X	X
12	Reliability reporting		X	X	X	X	X	X

Only 1 study presented separate DS, MS, and FS data, thus not allowing data synthesis. Substantial heterogeneity was present for DMFT and MT while other outcomes showed less heterogeneity. For deciduous teeth, data from 4 studies with a total sample size of 321 suggest that CLP patients have a higher dmft than the control, with a mean difference of 1.51 ($p = 0.03$). Only 1 study presented separate dt, mt, and ft data, and similarly only 1 study presented dmfs data, therefore data synthesis was not possible. Substantial heterogeneity was present for the dmft results.

The risk of bias across studies using funnel plots was difficult to assess due to the limited number of studies. Visual inspection of funnel plots, however, did appear to suggest that between-study bias may be present to some extent.

Discussion

The results from the present study, using meta-analysis methodology, suggest that individuals with CLP tend to present with higher DMFT and dmft scores than matched non-CLP controls. When looking at caries prevalence in CLP patients, most studies pool all children into one group, regardless of cleft type. This does not allow for a precise assessment of caries prevalence in individual cleft types. Nevertheless, general epidemiological surveys are important for gaining knowledge about the prevalence of diseases in a population, and information obtained from these surveys can be used for health care planning [Agbaje et al., 2012]. The implications of the present study for the dentist/orthodontist dealing with cleft patients are that there should be a focus on education and motivation of both patients and parents, prevention, as well as more frequent recalls. Future studies, where investigators stratify data based on cleft type, will allow for a more precise evaluation of caries experience in the various cleft subgroups, and a more appropriate allocation of resources.

Agbaje et al. [2012] state that standardization of working methods is needed in order to assure the repeatability, comparability and validity of results obtained by different groups of subjects or by the same group over time. For assessing caries experience, different standardization criteria have been developed by different authorities, including the British Association for the Study of Community Dentistry [Pitts et al., 1997], the World Health Organization [WHO, 1997], and the International Caries Detection and Assessment System [Pitts, 2004]. In the present

Fig. 2. Forrest plots representing DMFT (**a**), DT (**b**), MT (**c**), FT (**d**), DMFS (**e**), and dmft (**f**), for CLP and matched non-CLP control patients. The studies listed in chronological order refer to studies summarized in table 1. Studies listed twice represent values for different age groups within an individual study. The diamonds represent the overall mean difference and 95% confidence intervals (CI). Shown below each forest plot are values for heterogeneity tests, as well as the significance of the overall effect.

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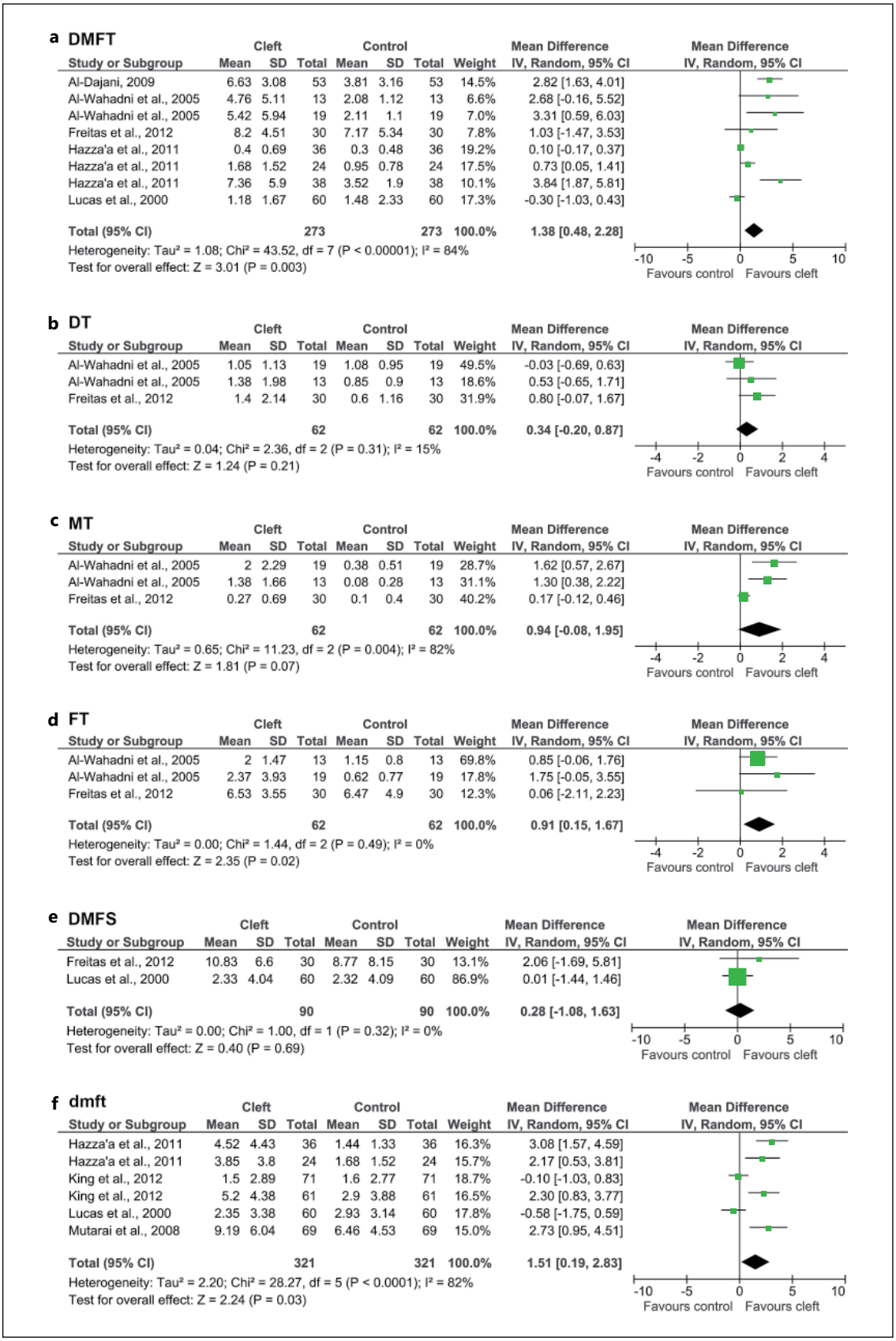

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study, the included studies all happened to use the WHO criteria, namely the decayed, missing, and filled teeth and/or surfaces indices. Agbaje et al. [2012] in their review of epidemiological surveys assessing caries experience noted that the WHO guidelines were not adhered to in many surveys, mainly for aspects such as the measurement and reporting of reliability measurement, type of probe, and light conditions. This finding was confirmed in the present study.

Clear and transparent reporting is a critical aspect of translating research findings to health care settings [Needleman et al., 2008]. When looking at the quality of reporting in individual studies, one can see that this varied, and the amount of information presented as regards the methodology in each study was often incomplete. It has been advocated that a report should contain enough and precise information to allow judgement of the validity of the results presented and of the conclusions reached, otherwise if reporting is inadequate, assumptions have to be made, and this could lead to a false interpretation [Agbaje et al., 2012].

Besides the transparency of the methods used, the reporting of the results should also be aimed to be as complete as possible. In the present investigation, only very few studies reported on the different components of the decayed, missing, and filled index. Most studies gave mean values for the whole index, without mentioning each of the individual components of the index. This information could be useful for health planning and management purposes.

Various explanations have been put forth as to why the presence of CLP predisposes individuals to develop more dental caries. CLP patients may have a compromised oral hygiene. The loss of elasticity due to the surgical reparation of the lip, the anatomy of the cleft, and the fear of toothbrushing around the cleft area have been suggested to lead to difficulties in achieving optimal oral health [Dahllöf et al., 1989]. Moreover, crowding which is often related to the higher incidence of supernumerary teeth and the limited arch space due to the underdevelopment of the maxilla can cause restricted access for the toothbrush and the natural cleansing of the teeth by the tongue and saliva [Johnsen and Dixon, 1984].

Food impaction may also be a problem in CLP patients in the presence of a palatal cleft and fistula, and food may escape through the nose and regurgitate into the mouth, potentially increasing the risk of caries development, as substrates for cariogenic bacteria are present in the mouth for longer periods of time [Ahluwalia et al., 2004; Cheng et al., 2007].

Enamel hypoplasia is another possible contributing factor to an increase in caries prevalence in CLP patients [Cheng et al., 2007]. CLP patients have been shown to have more frequent enamel hypoplasia of the incisor teeth adjacent to the cleft [Dixon, 1968], although Kirchberg et al. [2004] did not find an increase in caries prevalence in the permanent incisors of CLP patients.

The use of a pre-surgical infant orthopaedic appliance has also been suggested to be related to higher prevalence of caries in CLP children. The appliance, made of acrylic, may facilitate early colonization of mutans streptococci and *Lactobacilli* [van Loveren et al., 1998]. Such early colonization has been shown to predispose the patients to an early onset of caries in the primary dentition [Bokhout et al., 1996b]. It has been shown that children with oral clefts treated with intra-oral appliances have a 7-fold chance of exhibiting dental caries at the age of 2.5 years relative to children with oral clefts without intra-oral appliances [Bokhout et al., 1996a].

CLP patients often require orthodontic treatment, sometimes in several phases over several years. Orthodontic appliances may be another reason for the increase in prevalence of dental caries in CLP patients [Cheng et al., 2007] in comparison with control patients where orthodontic treatments are usually more straightforward and of a shorter duration.

Socioeconomic status is also an important risk factor in the development of dental caries. Parents of lower socioeconomic status are more likely to have CLP children [Mossey et al., 2011]. Likewise, lower socioeconomic status is related to an increased prevalence of dental caries [Reisine and Psoter, 2001], bringing to light the issue of inequalities in health. Finally, the importance of oral hygiene and dietary restrictions in individuals with CLP may not be of high priority for CLP children and their parents alike. Parents may reward their children with sweet foods or drinks, providing these to comfort their children in an attempt to be compassionate towards them given the CLP. Moreover, children with CLP may respond to mockery, which they may be subject to in school because of their dental malpositions, with less of an interest in their oral hygiene.

In conclusion, individuals with CLP, when compared with matched non-CLP controls, tend to have a higher prevalence of dental caries, as detected using the decayed, missing, and filled index. This holds true both for permanent and for deciduous teeth. One must keep in mind, however, that relatively few studies were

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included in the present meta-analysis, and the reporting on the methods in the individual studies was not always transparent.

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Conceived and designed the meta-analysis: G.A., G.H. Performed the literature search, data collection, and data synthesis: G.A., P.P. Wrote the paper: G.A., P.P., G.H.

Declaration of Interest

The authors declare that they have no conflicts of interest.

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