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ORIGINAL ARTICLE

Dental arch spatial changes after premature loss of first primary molars: a systematic review of controlled studies

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Abstract Studies investigating dental arch spatial changes following first primary molar premature loss are controversial regarding clinical significance. The purpose of this review was to systematically investigate the relevant literature. Controlled studies investigating changes before and after premature loss of first primary molars were searched in various databases. Split-mouth design studies were considered eligible for inclusion. The risk of bias was judged according to ADA Clinical Practice Guidelines. Only two analyzable split-mouth studies on mandibular first primary molar loss were identified. Space loss in the extraction side was greater at 2, 4, 6 and 8-month follow-ups, reaching a −1.5 mm difference in the final examination (95% Confidence Interval: −2.080 to −0.925; $p = 0.000$; random effects model). Studies were judged to be at unclear risk of bias. The amount of space decrease after premature loss of first primary molars may have management implications under certain circumstances. Comprehensive assessment of the various characteristics of each patient should precede management decisions in individual cases.

Keywords Primary first molars · Premature loss · Extraction · Arch changes · Systematic review

Introduction

Despite continuing reduction in its prevalence and severity, child dental caries still constitutes a major public health problem in many countries, often leading to the necessity of primary teeth extraction prior to natural exfoliation [1]. Premature loss of primary teeth has the potential to cause, or in conjunction with other growth and development influencing factors to increase needs for orthodontic treatment [2–9]. This is because premature loss of primary teeth in the developing dentition may result in a decrease of the space available for either the accommodation of permanent teeth or the management of preexisting occlusal and/or dentoalveolar discrepancies [3]. A recent study using the Index of Orthodontic Treatment Need (IOTN), calculated that each prematurely extracted primary tooth led to an 18% increase in malocclusion warranting intervention in the United Kingdom's National Health Service [10]. Thus, the maintenance of primary teeth throughout the transition from primary to full permanent dentition has been suggested as being particularly important in preventing arch space loss and in limiting the eventual malocclusion and the subsequent necessity or complexity for orthodontic management [11, 12].

Regarding the second primary molar, it has long been maintained that its premature loss may be detrimental for the developing dentition [8, 13–15]. However, studies investigating first primary molar premature loss are more controversial regarding its clinical significance [8, 9, 16, 17], especially if extraction has taken place after the eruption of the first permanent molars [13, 14, 17].

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This lack of consensus on the need of space maintenance in such cases poses the need for generation of evidence-based information to support treatment decisions. An earlier systematic review concluded on small short-term space loss following the premature loss of first primary molars but no attempt was made to summarize quantitatively the relevant observations [18]. The purpose of this study was to systematically investigate the available literature, including a search for more recent data, regarding dental arch spatial changes following premature loss of first primary molars.

Materials and methods

The present systematic review was carried out according to a preexisting protocol following the guidelines outlined in the PRISMA statement [19], the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0) [20] and the ADA Clinical Practice Guideline methodology [21]. No funding was received for the present project.

Selection criteria applied for the review

Since early extraction is the main cause of premature loss of primary molars [10], studies investigating dental arch changes before and after maxillary or mandibular first primary molar extraction, earlier than normal exfoliation were reviewed [22]. Split-mouth design studies, comparing dental arch changes before and after a unilateral extraction, were considered eligible for inclusion.

All studies should fulfill certain criteria on participants' and intervention characteristics, as well as outcomes measured.

- Types of participants: this search included studies on patients with first permanent molars about to erupt or already erupted, as dental arch spatial changes after this specific dental development stage may be less pronounced [5, 14, 17].
- Types of interventions: the search aimed at including studies where a group of children with maxillary or mandibular first primary molar early extraction was compared to a group without extraction, to account for normal growth changes. For the split-mouth studies, studies where the unilateral early extraction quadrant was compared to the unaffected contralateral, thus serving as control, were considered. In addition, studies where no space maintenance and/or regaining appliances or other similar interventions were considered.
- Outcome measures: the outcomes of interest were the average difference between the intervention and control groups (or the intervention and the control side, for the split-mouth studies) in the change of available space in the extraction area, arch width, length and perimeter (together with the respective measure to quantify the amount of dispersion of the set of data values). Studies measuring outcomes immediately before or after tooth loss and at specified time points during the follow-up period were included, as both common sense and studies suggest that a temporal relationship may exist between tooth removal and the various outcomes [8, 23–26].

From the present systematic review, animal studies, non-comparative studies (case reports and case series), reviews (traditional reviews, systematic reviews and meta-analyses), as well as opinion articles were excluded. Also studies including premature extraction of permanent tooth or teeth, studies investigating normal primary teeth exfoliation, as well as, cross-sectional studies and studies where the post-extraction follow-up interval was impossible to be identified accurately were not considered. In these cases, it is not possible to chronologically relate the effect of tooth loss on the spatial change outcome. This inability may be crucial as present data suggests that space changes continue over the course of time [8, 23–26].

Search strategy for identification of studies

The first author developed detailed search strategies for each database searched. They were based on the strategy developed for MEDLINE but revised appropriately for each database to take account of differences in controlled vocabulary and syntax rules. The following electronic databases were searched up to December 31st, 2015 (Appendix, Table 3): MEDLINE (via PubMed), the Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews, Scopus, Web of Science Core Collection, as well as, regional sources such as LILACS, IndMed and Arab World Research Source. Grey literature was searched on Google Scholar, ClinicalTrials.gov, and ProQuest Dissertations and Theses Global database.

No restrictions on the language and date of publication were placed. Also the reference lists of all eligible studies for additional studies were utilized. Where additional information on some publication was necessary, attempts were made for contacting the respective authors.

Selection of studies and data extraction

The second and third authors assessed the retrieved records for inclusion independently, without being blinded to the identity of the authors, their institution, or the research results. They obtained and assessed, again independently, the full report of publications considered by either reviewer to meet the inclusion criteria. Disagreements were resolved by discussion or consultation with the first author. Record of all decisions on study identification was kept.

The same two authors performed data extraction independently and any disagreements were again resolved by discussion or consultation with the first author. Data collection forms were used to record the desired information, like bibliographic details, details on study design, verification of study eligibility, participant and intervention characteristics, patient attrition and the respective reasons, outcomes assessed and assessment procedures. In case of need for clarifications on the published data or additional material, attempts were made to contact the corresponding authors.

Data synthesis and assessment of publication bias

In cases of appropriate data, the random effects method for meta-analysis was used to combine space changes across studies [27, 28], because of the expected clinical diversity.

To identify the presence and extent of between-study heterogeneity, the overlap of the 95% CI for the results of individual studies was inspected graphically and Cochrane's test for homogeneity and the I^2 statistic were calculated [20]. If deemed possible, exploratory subgroup analyses were planned according to participant characteristics. In addition, if a sufficient number of trials were identified, analyses were planned for "small-study effects" and publication bias [20].

All analyses were done with Comprehensive Meta-analysis software 2.2.046 (©2007 Biostat Inc.). Significance (α) was set at 0.05, except for a 0.10 used for the heterogeneity tests [29].

Assessment of risk of bias

First and last authors assessed the risk of bias in the included studies independently, using the ADA Clinical Practice Guideline methodology [21]. Any disagreements were resolved by discussion and consensus. The criteria examined included selection of participants, confounding, attrition and missing data, measurement of interventions and outcomes, as well as consideration and report of important outcomes. Studies were finally given a characterization of low risk of bias (study meets all of the criteria), unclear risk of bias (study fails to meet or it is unclear that it meets at least one criterion, but does not have a fatal flaw), and finally high risk of bias (study has at least one fatal flaw).

Results

The flow of records through the reviewing process is shown in Fig. 1. The search initially identified 6283 records and subsequently 3356 were excluded as duplicates and 2891 more on the basis of their title and abstract. From the 36 records that remained and were assessed in full-text, 34 were excluded for various reasons (12 studies irrelevant to the review scope, seven studies with inadequate or inappropriate statistical information, three retrospective studies, three studies where the exact timing of cast measurements relative to the extraction could not be identified, two studies without measurements before the extractions, two cross-sectional studies, one study investigating a mixed population of maxillary and mandibular first primary molar extractions; one investigating the effect of both extractions and caries; one study with no control group, one study where some of the participants lacked the pre-extraction cast and one study that involved patients long before the eruption of first permanent molars).

Finally, two full-text trial reports on mandibular first primary molar premature loss fulfilled the criteria to be included in the present review [30, 31]. No data on comparative space changes could be obtained for the case of the maxillary first primary molars, as the retrieved studies did not include enough statistical information on the variation of the data sets to enable quantitative synthesis.

Study characteristics and risk of bias assessment

The characteristics of the studies included in the present systematic review are presented in Tables 1 and 2. The papers had been published in 1998 and 2006 and were of the split-mouth design investigating dental arch changes before and after a unilateral premature extraction in the test quadrant compared to the unaffected control one.

The studies analyzed children aged between 5.1 and 9 years originating from clinics providing pediatric dental services. Fifty-one children underwent extraction of a mandibular first primary molar and were followed for up to 8 months [30, 31]. The retrieved studies did not report a priori calculating of sample size and the study by Padma Kumari and Retnakumari [31] had dropouts but did not carry out an intention-to-treat analysis.

Dental arch changes were measured on casts from alginate impressions taken immediately before or after the extraction and at specific time points there after. Only dental arch changes in the unilateral extraction quadrant compared to control measurements in unaffected contralateral were included in the present review; D + E space [30] and D space [31]. Other measurements such as arch width, length and perimeter changes in the extraction

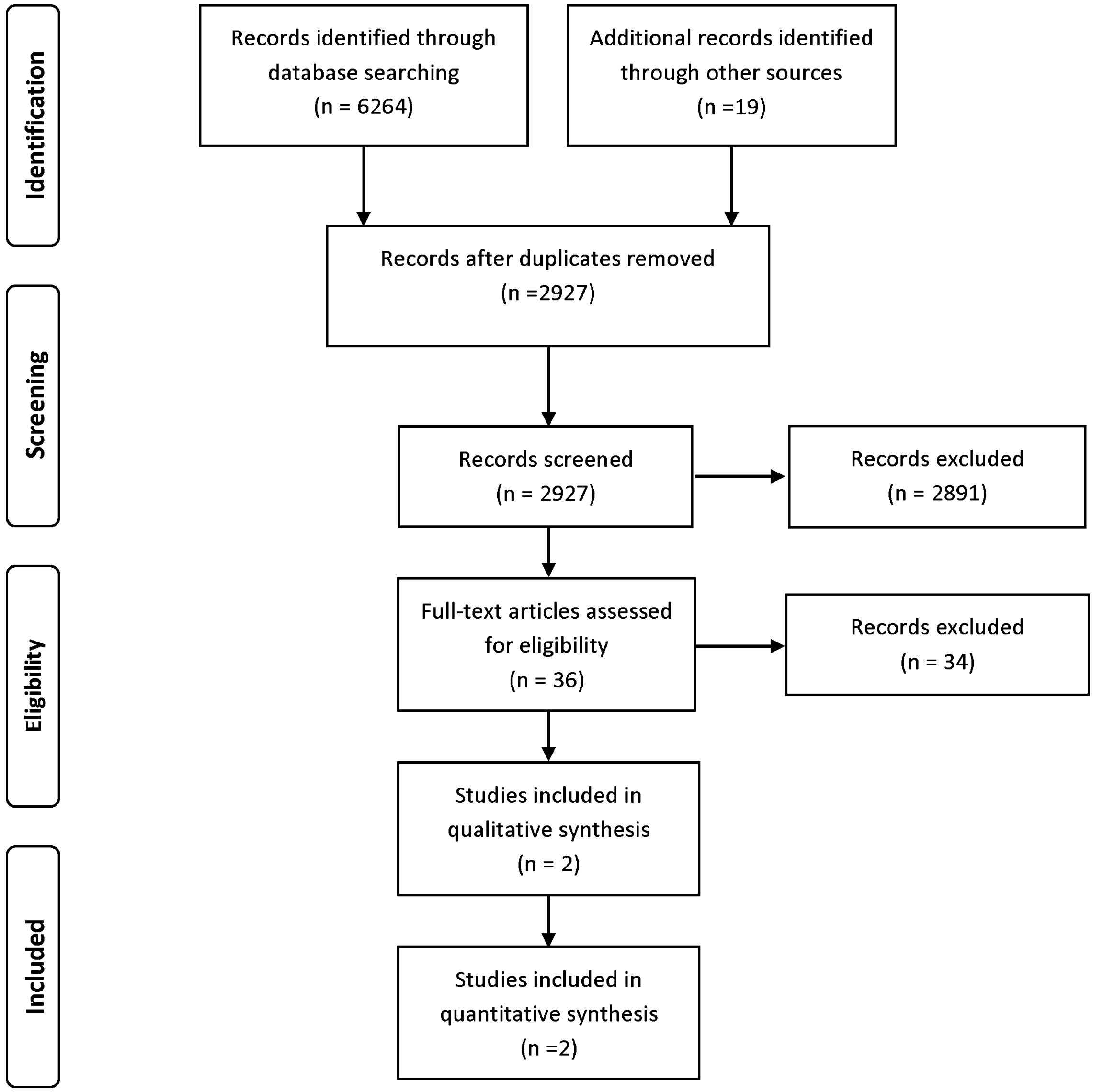

Fig. 1 Flow diagram of the retrieved studies through the selection process

arches could not be included because they were not compared to a group without extraction to account for normal growth changes.

Regarding the risk of bias in the included studies, all were judged to be at unclear risk, as they failed to meet some criteria, but did not have fatal flaws. Most problems were encountered with regards to confounding, as they missed considering confounding factors, such as space conditions in the arch or the dental age stage. Risk of bias in the measurement of outcomes was in general assessed as moderate because blinding was not possible. Bias from missing data in the present context was judged as low in the study that reported dropouts [31]. Finally, the risk was considered low for the criteria regarding the selection of the participants for the study, the measurement of interventions, as well as for the consideration and report of important outcomes.

Dental arch spatial changes

The results of the studies included in the present review are summarized in Fig. 2. The authors were unable to examine publication and reporting biases, or conduct subgroup analyses, due to the limited number of relevant studies retrieved. The measured space loss in the premature first primary molar extraction site was greater than the control side at 2, 4, 6 and 8-month follow-ups, amounting to 1.5 mm space difference in the final examination [95% confidence interval (95% CI): −2.080 to −0.925; $p = 0.000$] [30, 31].

Table 1 General characteristics of the studies included in the systematic review

Study	Design and intervention	Outcomes included and measurements	Other issues
Lin and Chang [30] Taiwan	Split-mouth Unilateral extraction of Md D	**D + E space:** distance between the mesial midpoint of the 6 (or distal midpoint of the E) and the distal midpoint of the C (measurement determined for both extraction and control sides) **Measurements on alginate casts** T_0: 2–3 days after the extraction T_1: 8 months approximately	**Sample size calculation:** No **Method error considerations:** One examiner. Measurements repeated twice. The error expressed as SD was 0.33 mm
Padma Kumari and Retnakumari [31] India	Split-mouth Unilateral extraction of Md D	**D space:** distance between the mesial midpoint of the E and the distal midpoint of the C (measurement determined for both extraction and control sides) **Measurements on alginate casts** T_0: immediately before the extraction T_1: 2 months T_2: 4 months T_3: 6 months T_4: 8 months	**Sample size calculation:** No **Method error considerations:** Measurements repeated 3 times and averaged

Md mandibular, *D* first primary molar, *E* second primary molar, *C* primary canine, *6* first permanent molar, *SD* standard deviation

Table 2 Participants' characteristics in the studies included in the systematic review

Study	Inclusion criteria	Patients recruited and analyzed
Lin and Chang [30] Taiwan	(1) 6s about to erupt or have erupted. (2) Patient cooperative in finishing dental treatment before taking the impression. (3) Unilateral premature loss of the Md D due to extensive decay, but intact opposite primary molars. (4) Absent permanent successor for at least two years after extraction of the primary molars. (5) Parents or guardians did not want to receive treatment of a space maintainer.	**Patients recruited:** 21 children (12 males; 9 females); Children's Dental Clinic of Chang Chung Memorial Hospital, Kaohsiung Medical Center, Taiwan; Age: mean: 6.11 years (range 5.1–7.2) at the time of extraction **Patients analyzed:** 21 children
Padma Kumari and Retnakumari [31] India	(1) 6s erupted. (2) Unilateral extraction of the Md D due to extensive decay and having intact anterior tooth. (3) Acceptable anteroposterior and lateral arch relationships. (4) Absent permanent successor for at least two years after extraction of the primary molars. (5) Parents and guardians who were willing to overweigh the effects of not maintaining the extraction space. (6) No space-maintaining appliance used.	**Patients recruited:** 40 children; Department of Pedodontics, Government Dental college, Thiruvananthapuram, India; age: 6–9 years at the time of extraction **Patients analyzed:** 30 children (10 lost to follow-up); age: 6–9 years at the time of extraction

Md mandibular, *D* first primary molar, *6* first permanent molar

Finally selected studies	N	Extraction Side Mean (±SD)	N	Control Side Mean (±SD)	Weight %	WMD, 95% CI
2 months follow-up						
Padma Kumari & Retnakumari, 2006	30	-0.58 (± 0.48)	30	-0.03 (± 0.13)		-0.550 [-0.728, -0,372]
Test for effect: Z = -6.058 (*p* = 0.000)						
4 months follow-up						
Padma Kumari & Retnakumari, 2006	30	-1.08 (± 0.56)	30	-0.05 (± 0.15)		-1.030 [-1.237, -0.823]
Test for effect: Z = -9.731 (*p* = 0.000)						
6 months follow-up						
Padma Kumari & Retnakumari, 2006	30	-1.58 (± 0.65)	30	-0.07 (± 0.17)		-1.650 [-1,890, -1,410]
Test for effect: Z = -13.451 (*p* = 0.000)						
8 months follow-up						
Lin & Chang, 1998	21	-1.22 (± 0.86)	21	-0.03 (± 0.11)	47.02	-1.190 [-1,561, -0,819]
Padma Kumari & Retnakumari, 2006	30	-1.85 (± 0.65)	30	-0.07 (± 0.17)	52.98	-1.780 [-2.020, -1.540]
Total	51		51		100.00	-1.503 [-2.080, -0.925]
Test for heterogeneity: Q-value = 6.847, df (Q) = 1 (*p* = 0.009), I² = 86 %						
Test for overall effect: Z = -15.598 (*p* = 0.000)						

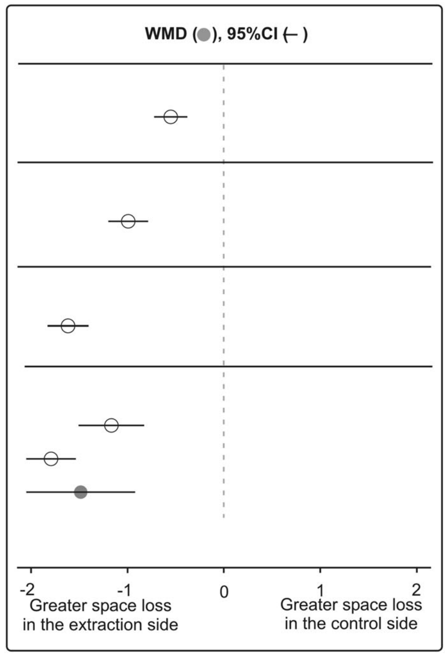

Fig. 2 Space changes in the extraction and control sides following of mandibular first primary molar loss prior to natural exfoliation

Discussion

Based on the findings of the present review that followed well-established guidelines, it seems that premature loss of mandibular first primary molars results in less space available in the extraction side compared to the control side. The observed space decrease could provide an initial guide useful in clinical setting, bearing in mind the small number of eligible trials, their heterogeneity with regards to patients' characteristics and method related factors, as well as the results of the risk of bias assessment. Given the multitude of parameters implicated in determining the clinical significance of space loss, comprehensive assessment of the various characteristics of each patient should characterize management decisions in individual cases.

The fact that only two studies satisfied the pre-specified criteria for inclusion in the present paper reflects the scarcity of useful relevant research. The consequent lack of extensive data is rather surprising, as space changes following loss of a primary first molar before natural exfoliation have been observed in varying degrees in the literature and the subsequent management remains a subject of debate. Although certain trends exist, the scientific data produced has been inconsistent and no attempt to quantitatively summarize the reported changes to produce values serving as guidance in clinical practice has been made [18]. As decreases in intra-arch space could influence various treatment decisions [3], the need for evidence-based information regarding dental arch spatial changes following loss of first primary molars prior to natural exfoliation, to support the care provided could be beneficial.

In addition, the paucity of research eligible for inclusion is a measure of how few trials met the inclusion criteria set. Many of the retrieved studies did not involve comparison with control data to account for normal growth changes, either in the form of a separate group or measurements from the contralateral unaffected site in cases of unilateral tooth loss. The existence of controls is important, as the observation of space change at the extraction site does not always imply that it is solely due to tooth loss. Moreover, spatial differences can also be observed in intact dental arches or those minimally affected by caries [8]. Thus, lack of consideration of normally expected tooth arch changes could result in over- or under-estimation of the spatial effects of tooth loss. As a result of the lack of controlled studies, no data on outcomes further to the space changes in the tooth loss area, such as arch width, length and perimeter, could be presented in the current review despite the fact that they were measured in the split-mouth studies included [30, 31].

Moreover, certain publications could not be included in data analysis because either they did not present information on the status prior to tooth loss or the post-loss follow-up interval could not be identified accurately. These incomplete data, as well as information from cross-sectional observations, result in difficulty in relating chronologically the exposure (i.e., tooth loss) to possible outcomes of interest, as both common sense and various studies suggest that a temporal relationship may exist between them [8, 23–26]. In other cases, the results from some studies that could have otherwise been included in the meta-analysis were not reported in a suitable format (i.e., space changes were assessed only as proportion of cases with space decrease) or accurately from statistical perspective. Thus, the absence of reporting the standard deviation of space loss or alternative statistics, as well as the lack of responses from the corresponding authors when contacted for additional data, consequently, excluded them from further consideration.

Based on the information retrieved during the present systematic review, in the case of loss of a mandibular first primary molar, more space is initially lost at the extraction site—at a rate of 0.25 mm per month—compared to the control side [31]. At the 8-month follow-up, quantitative data synthesis revealed statistically significantly less space of −1.5 mm with 95% CI for the space loss ranging from −2.080 to −0.925 mm [30, 31]. Although such quantitative syntheses can only be regarded as exploratory until additional research becomes available, current concepts support that data from even as few as two studies can be combined, provided that these can be meaningfully pooled [32], as all other summarizing techniques are less transparent and/or are less likely to be valid [33]. In addition, it has been suggested that any amount of heterogeneity is acceptable, provided that the eligibility criteria for the meta-analysis are sound and that the data are correct [34, 35]. Thus, the heterogeneity observed in the space decrease result is to be anticipated. It would be extraordinary if multiple studies, performed by different teams in different places with non-identical methods, ended up estimating the same underlying parameter [35].

In the context of the present review, heterogeneity can arise from diversity in terms of patients' characteristics (i.e., age, ethnicity, etc.), as well as method related factors and was incorporated in a justifiable random effects model. As the oral cavity constitutes an ever-changing environment, the position of the various landmarks may be modified by factors such as tooth eruption, caries, restorations, attrition and growth [36]. Thus, the use of stable reference points in the measurements is preferable for reaching conclusions on the possible mechanisms associated with the change [37–39]. Moreover, the accuracy of measurements on plaster models may be limited owing to both possible distortions of the plaster models, as well as method error considerations associated with the manual measurement technique [36].

Heterogeneity can also arise from variability in their conduct. In the present review, both studies included were classified as having an unclear overall risk of bias; meaning that they failed to meet or it was unclear that they met at least one criterion, but did not have a fatal flaw. The observed problems were mainly related to confounding, as they missed considering factors such as space conditions in the dental arch and the variety in the eruption stage of the first permanent molars. Risk of bias in the measurement of outcomes was in general assessed as moderate because blinding was not possible and follow-up periods were not long enough to develop a broader understanding of the spatial effects of the primary first molar extraction. Bias from missing data in the present context was judged as low in the study that reported dropouts [31]. Finally, the risk was considered low for the criteria of the selection of the participants, measurement of interventions, as well as, consideration and report of important outcomes.

In considering the clinical relevance of the results demonstrated in the present review, one should acknowledge that the ultimate effect of the premature loss of primary teeth can be modified by factors, such as eruption sequence and time, skeletal and muscular characteristics, periodontal factors and craniofacial growth [25]. Furthermore, the direction, magnitude and the speed of movement may vary among individuals depending on extraction timing, space condition and intercuspation [5, 13, 14, 28, 40]. In general, under conditions of normally evolving dentoalveolar and occlusal relationships, the presented mean values for the space lost may not have implications, because of the existence of the leeway space. However, the magnitude of the leeway space is not consistent and may vary greatly from person to person [41, 42]. Moreover, space deficiency may not always be apparent as it can manifest in forms other than crowding. For example, an increased curve of Spee and/or teeth protrusion constitute situations of lack of space that, if they are combined with some degrees of apparent crowding or lip protrusion, may constitute complex problems that warrant intervention. Under such conditions, the amount of space loss demonstrated in the present review could have treatment implications with regards to anchorage management or the need of tooth extraction [3].

Thus, the clinical significance of space lost and the need for space maintenance may only be determined after comprehensive assessment of the various characteristics of each individual case and should not be considered only in view of apparent severe crowding. It is more sensible to weigh carefully the possible broader detrimental intra-arch and dentoalveolar effects, as well as, the possible changes in general orthodontic treatment planning and differentiation of anchorage needs in case of future orthodontic intervention that may be brought about by uncontrolled tooth drift. At the same time, these effects should be balanced against considerations regarding the long-term survival of space maintainers [43–45] and their potential adverse effects in terms of plaque retention and increased risk for developing caries and gingival inflammation that logically follows where a patient does not present acceptable plaque control [46, 47]. Patient's ability to cooperate and poor oral hygiene should still concern the clinician on the appropriateness of fixed space maintainers. However, the use of fluoride releasing glass ionomer luting cements and their newer developments have shown to have greatly combatted the problem of caries under cemented bands [48, 49]. It is appropriate that caries risk is taken into account and an individualized caries prevention program and recall schedule is applied [46, 50–52] for the added reason of assessing the integrity of the appliance, the condition of the abutment teeth and the general development of the dental arches and the occlusion [53, 54].

As the results of this study constitute an initial guide, additional future research is required to further clarify the effect of the premature extraction of primary first molars. As randomized controlled trial designs may involve ethical considerations, prospective, adequately powered studies of children with premature loss of primary teeth with follow-up until the establishment of full permanent dentition are required. Ideally, such studies should adjust for the various confounders and have as a primary outcome measure malocclusion, measured by a valid, reliable, reproducible and widely used index. The assessment of malocclusion is important not only because in that way one may consider the broader intra- and inter-arch effects of primary loss of teeth, but also because a decrease in treatment need and complexity is important from the quality of life perspective [55, 56]. Of course, secondary outcome measures could include various measurements used to quantify spatial relationships in the dental arch, but should ideally use stable reference points because of the ever-changing nature of the developing dentition.

In conclusion, although the formation of definite guidelines in not possible, the included data constitute initial guidance that mandibular first primary molar premature loss results in less space available in the extraction side compared to the control site. This finding could have management implications under certain circumstances. Thus, good practice would suggest comprehensive assessment of the various characteristics of each case before confirming or negating the necessity for space maintenance.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Appendix

See Table 3.

Table 3 Databases searched, search strategy and respective hits

Database	Search strategy	Hits
General sources		
MEDLINE via PubMed http://www.ncbi.nlm.nih.gov/pubmed	(((((((molar[Title/Abstract]) OR molars[Title/Abstract]) OR tooth[Title/Abstract]) OR teeth[Title/Abstract])) AND ((primary[Title/Abstract]) OR deciduous[Title/Abstract])) AND (((((((loss[Title/Abstract]) OR extract[Title/Abstract]) OR extraction[Title/Abstract]) OR extracted[Title/Abstract]) OR exfoliate[Title/Abstract]) OR exfoliation[Title/Abstract]) OR exfoliated[Title/Abstract])) AND (((((((((((((migration[Title/Abstract]) OR drift[Title/Abstract]) OR drifting[Title/Abstract]) OR space[Title/Abstract]) OR arch[Title/Abstract]) OR change[Title/Abstract]) OR changes[Title/Abstract]) OR eruption[Title/Abstract]) OR position[Title/Abstract]) OR closure[Title/Abstract]) OR effect[Title/Abstract]) OR effects[Title/Abstract]) OR result[Title/Abstract]) OR results[Title/Abstract])	920
Cochrane Central Register of Controlled Trials http://onlinelibrary.wiley.com/cochranelibrary/search	(molar OR molars OR tooth OR teeth) AND (primary OR deciduous) AND (loss OR extract OR extraction OR extracted OR exfoliate OR exfoliation OR exfoliated) AND (migration OR drift OR drifting OR space OR arch OR change OR changes OR eruption OR position OR closure OR effect OR effects OR result OR results) in Title, Abstract, Keywords in Trials'	409
Cochrane Database of Systematic Reviews http://0-ovidsp.tx.ovid.com.amclb.iii.com/sp-3.16.0b/ovidweb.cgi	(molar OR molars OR tooth OR teeth) AND (primary OR deciduous) AND (loss OR extract OR extraction OR extracted OR exfoliate OR exfoliation OR exfoliated) AND (migration OR drift OR drifting OR space OR arch OR change OR changes OR eruption OR position OR closure OR effect OR effects OR result OR results) {Including Limited Related Terms}	1

Table 3 continued

Database	Search strategy	Hits
Scopus https://www.scopus.com/search/form.url?zone=TopNavBar&origin=searchbasic	(TITLE-ABS-KEY (molar OR molars OR tooth OR teeth) AND TITLE-ABS-KEY (primary OR deciduous) ANDTITLE-ABS-KEY (loss OR extract OR extraction OR extracted OR exfoliate OR exfoliation OR exfoliated) AND TITLE-ABS-KEY (migration OR drift OR drifting OR space OR arch OR change OR changes OR eruption OR position OR closure OR effect OR effects OR result OR results)) AND (LIMIT-TO (SUBJAREA, "DENT"))	2389
Web of Science™ Core Collection http://apps.webofknowledge.com/	TOPIC: ((molar OR molars OR tooth OR teeth) AND (primary OR deciduous) AND (loss OR extract OR extraction OR extracted OR exfoliate OR exfoliation OR exfoliated) AND (migration OR drift OR drifting OR space OR arch OR change OR changes OR eruption OR position OR closure OR effect OR effects OR result OR results)) Refined by: RESEARCH AREAS: (DENTISTRY ORAL SURGERY MEDICINE) Timespan: All years. Search language = Auto	1567
Regional sources		
LILACS http://lilacs.bvsalud.org/en/	(molar OR molars OR tooth OR teeth) AND (primary OR deciduous) AND (loss OR extract OR extraction OR extracted OR exfoliate OR exfoliation OR exfoliated) AND (migration OR drift OR drifting OR space OR arch OR change OR changes OR eruption OR position OR closure OR effect OR effects OR result OR results)	170
IndMed http://indmed.nic.in/indmed.html	(molar OR molars OR tooth OR teeth) AND (primary OR deciduous) AND (loss OR extract OR extraction OR extracted OR exfoliate OR exfoliation OR exfoliated) AND (migration OR drift OR drifting OR space OR arch OR change OR changes)	15
Arab World Research Source http://0-web.a.ebscohost.com.amclb.iii.com/ehost/search/advanced?sid=ff64c697-1ea0-41dc-9afe-961bc654cd05%40sessionmgr4002&vid=0&hid=4114	(loss OR extract OR extraction OR extracted OR exfoliate OR exfoliation OR exfoliated) AND (migration OR drift OR drifting OR space OR arch OR change OR changes OR eruption OR position OR closure OR effect OR effects OR result OR results	180
Grey literature sources		
Google Scholar https://scholar.google.com	1. Allintitle: molars primary loss OR extract OR extraction OR extracted OR exfoliate OR exfoliation OR exfoliated 2. Allintitle: molar primary loss OR extract OR extraction OR extracted OR exfoliate OR exfoliation OR exfoliated 3. Allintitle: molar deciduous loss OR extract OR extraction OR extracted OR exfoliate OR exfoliation OR exfoliated 4. Allintitle: molars deciduous loss OR extract OR extraction OR extracted OR exfoliate OR exfoliation OR exfoliated	46 69 25 75
ClinicalTrials.gov http://clinicaltrials.gov/	(molar OR molars OR tooth OR teeth) AND (primary OR deciduous) AND (loss OR extract OR extraction OR extracted OR exfoliate OR exfoliation OR exfoliated) AND (migration OR drift OR drifting OR space OR arch OR change OR changes)	229
ProQuest Dissertations & Theses Global http://search.proquest.com	(molar OR molars OR tooth OR teeth) AND (primary OR deciduous) AND (loss OR extract OR extraction OR extracted OR exfoliate OR exfoliation OR exfoliated) AND (migration OR drift OR drifting OR space OR arch OR change OR changes OR eruption OR position OR closure OR effect OR effects OR result OR results); Subject: dentistry; Index term (keyword): [Clear(Clear Index term (keyword)) Index term (keyword)]: Orthodontics OR Children OR Pediatric dentistry OR Teeth OR Malocclusion OR Orthodontic OR Cephalometric OR Crowding	169

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