**abstract**

**CONTEXT:** Symptoms associated with the primary tooth eruption have been extensively studied but it is still controversial.

**OBJECTIVE:** To assess the occurrence of local and systemic signs and symptoms during primary tooth eruption.

**DATA SOURCES:** Latin American and Caribbean Health Sciences, PubMed, ProQuest, Scopus, and Web of Science were searched. A partial gray literature search was taken by using Google Scholar and the reference lists of the included studies were scanned.

**STUDY SELECTION:** Observational studies assessing the association of eruption of primary teeth with local and systemic signs and symptoms in children aged 0 to 36 months were included.

**DATA EXTRACTION:** Two authors independently collected the information from the selected articles. Information was crosschecked and confirmed for its accuracy.

**RESULTS:** A total of 1179 articles were identified, and after a 2-phase selection, 16 studies were included. Overall prevalence of signs and symptoms occurring during primary tooth eruption in children between 0 and 36 months was 70.5% (total sample = 3506). Gingival irritation (86.81%), irritability (68.19%), and drooling (55.72%) were the most frequent ones.

**LIMITATIONS:** Different general symptoms were considered among studies. Some studies presented lack of confounding factors, no clear definition of the diagnostics methods, use of subjective measures and long intervals between examinations.

**CONCLUSIONS:** There is evidence of the occurrence of signs and symptoms during primary tooth eruption. For body temperature analyses, eruption could lead to a rise in temperature, but it was not characterized as fever.

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Dr Massignan worked on study conceptualization, design, data collection, data analysis, drafted the initial manuscript, and critically reviewed manuscript; Drs Cardoso and Porporatti worked on data analysis, and reviewed and revised the manuscript; Dr Aydinoz worked on data analysis and critically reviewed the manuscript; Drs De Luca Canto and Mezzomo worked on study conceptualization, design, data analysis, and critically reviewed manuscript; Dr Bolan worked on study conceptualization, design, data collection, data analysis, and critically reviewed manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

**DOI:** 10.1542/peds.2015-3501

Accepted for publication Nov 23, 2015

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Tooth eruption is a physiologic process in which teeth move from their development position within the alveolar bone to break the gum toward the oral cavity. Nevertheless, this mechanism and the source of the eruptive force has not been established nor completely understood. Despite being a natural process of child development, the impacts of primary tooth eruption on the overall health of children are still controversial. Recent studies have suggested that tooth eruption could be accompanied by different benign symptoms, such as increased salivation, irritability, loss of appetite for solid foods, and rise in body temperature. Moreover, the eruption of primary teeth has been assumed among parents to be associated with behavioral and systemic changes. The period of time that tooth eruption occurs can be very frustrating and stressful for parents, especially when it happens to their first offspring. Many parents do not know how to identify the signs of tooth eruption in their children and, therefore, do not feel confident to relieve the discomfort of the child. Likewise, many health professionals also believe that there is an association between some signs and symptoms and the eruption of primary teeth. Surveys with pediatricians and other child health professionals showed that these beliefs are common. The use of this diagnostic label may lead to either parents not managing the eruption of their child or the doctors to ignore significant symptoms and fail in diagnoses. Nevertheless, consistent evidence on the association of tooth eruption and general signs and symptoms are rather low and out of date. In a review conducted by Tighe et al in 2007 to identify the existence of any pathognomonic sign and symptom of dental eruption, a variety of symptoms that may occur simultaneously with the tooth eruption was demonstrated and no evidence suggested the existence of any signs or symptoms that could predict the tooth eruption.

Thus, the purpose of this systematic review was to answer the following focused question: “In children aged 0 up to 36 months, are there local or systemic signs and symptoms during the eruption of the primary teeth?”

**METHODS**

This systematic review was oriented following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol. Protocol Registration

The systematic review protocol was recorded at the International Prospective Register of Systematic Reviews under number CRD 42015020822.

**Inclusion Criteria**

Observational studies assessing the occurrence of local and systemic signs and symptoms during the spontaneous eruption of primary teeth in healthy children aged between 0 and 36 months, by means of either clinical examination or a questionnaire directed to the parents or health care professionals, were included. The local and systemic signs and symptoms evaluated were all reported complications related to teething described in the studies (eg, decreased appetite, diarrhea, drooling, fever, inflammation, swelling, vesicles or ulceration of the gum, irritability, rash, rhinorrhea, sleeping disturbances, vomiting).

Exclusion Criteria

Exclusion of the studies was performed in 2 phases. In phase 1 (titles and abstracts), the exclusion criteria were as follows: (1) studies conducted in children aged >36 months old; (2) reviews, letters, conference abstracts; (3) studies in which the sample included patients with genetic syndromes (eg, Down syndrome, craniofacial anomalies, neuromuscular disorders); (4) studies in which the sample included malignancies, malnutrition, and chronic diseases; (5) studies in which the sample included nonsprontaneous eruption of primary teeth; and (6) studies in which the eruption of primary teeth was not the primary outcome. Besides the 6 cited criteria, in phase 2 (full-test) the following exclusion criteria were added: (7) studies in which clinical examination was not performed by a health care professional, and (8) articles that evaluated the same sample.

**Information Sources and Search Strategies**

A systematic search was conducted on the following electronic databases: Latin American and Caribbean Health Sciences (LILACS), PubMed, ProQuest Dissertations and Theses Database, Scopus, and Web of Science, for titles and abstracts relevant to the research question. The syntax has been adapted to each database (Supplemental Appendix 1). A partial gray literature search was taken using Google Scholar limited to the first 100 most relevant articles published in the past 5 years. The reference lists of the included articles were scanned to identify additional studies of relevance. All references were managed by reference manager software EndNote Basic (Thomson Reuters, New York, NY) and duplicate hits were removed. The end search date was May 6, 2015. No language or date restrictions were applied.

**Study Selection**

The selection occurred in a 2-phase process to minimize bias. In phase 1, studies were independently screened by 2 reviewers (CM, MB) based on the titles and, if available, the abstracts derived from the search. Any study that clearly did not fulfill...
the inclusion criteria was discarded. In phase 2, the full text of relevant papers was retrieved for further analysis by the same 2 reviewers (CM, MB) and was either included or excluded for review on the basis of the eligibility criteria. Disagreements of inclusion/exclusion were handled through discussion, and the third reviewer (MC) was consulted to make a final decision.

**Data Collection Process**

Two authors (CM, MB) independently collected the required information from the selected articles. After that, all the collected information was crosschecked and confirmed for its accuracy. Again, any disagreement was resolved by discussion and mutual agreement between the authors. The third author (MC) was involved, when required, to make a final decision.

**Data Items**

For all of the included studies, the following structured information was recorded: study characteristics (authors, year of publication, country, study design, setting), population characteristics (sample size, age of participants), intervention characteristics (type of diagnostic approach: clinical examination, body temperature, questionnaire) and, finally, outcome characteristics (assessed teeth, symptoms, mean temperature in noneruption days, mean temperature in eruption days, and conclusions pertaining to the occurrence of local and systemic signs and symptoms during the eruption of primary teeth). Authors were contacted for further details when relevant information was not reported or there was doubt remaining about duplicate publication.

**Risk of Bias in Individual Studies**

Two reviewers (CM, MB) independently assessed the methodological quality of the included studies, using the "Quality in Prognosis Studies Tool" (QUIPS). The QUIPS tool comprises 6 domains: study participation, study attrition, prognostic factors measurement, outcome measurement, study confounding and statistical analysis and reporting to guide ratings of high, moderate, or low risk of bias. Disagreements were resolved through consensus when possible, or a third reviewer (MC) made the final decision.

**Summary Measures**

Presence of local and systemic signs and symptoms and differences in body temperature during the eruption of primary teeth were considered the main outcomes. For body temperature, the threshold point was considered according to a recent meta-analysis on accuracy of infrared tympanic thermometry, between 37.4°C and 37.8°C for tympanic temperature and 38.0°C for rectal temperature. Any type of related outcome measurement was computed (categorical variables and continuous variables).

**Synthesis of Results**

A meta-analysis was planned within the studies presenting enough data. The occurrence of signs and symptoms of the eruption of primary teeth was analyzed by 2 types of meta-analysis, for fixed and random effects following the appropriate Cochrane Guidelines. Meta-analysis was performed with the aid of MedCalc Statistical Software version 14.8.1 (MedCalc Software, Ostend, Belgium). Heterogeneity was calculated by inconsistency indexes (I²), and a value >50% was considered an indicator of substantial heterogeneity between studies. The significance level was set at 5%.

**Risk of Bias Across Studies**

Clinical heterogeneity (differences in participants, interventions, and outcomes) and methodological heterogeneity (study design, risk of bias) were explored.

**RESULTS**

**Study Selection**

The search identified 1318 citations across 5 databases. After duplicates removal, 1179 articles were screened in phase 1. A total of 65 articles met criteria for full-text screening. Additionally, 100 citations from Google Scholar were considered. From these, 4 further studies met the inclusion criteria. A hand search on the reference lists was performed for any study that might have been inadvertently missed by the electronic search procedures and 6 additional references were identified. Based on exclusion criteria for phase 2 (full-text screening), 59 articles were excluded. Two articles evaluated the same sample and 1 was not found. The reasons for exclusion are compiled in a comprehensive list (Supplemental Appendix 2). Therefore, 16 articles were selected for data collection with the aim of answering the review question. A flowchart of the process of identification and selection of studies is shown in Fig 1.

**Study Characteristics**

Research was conducted in 8 different countries: Australia, Brazil, Colombia, Finland, India, Israel, Senegal, and United States. The sample size ranged widely from 16 to 1165 children. The search involved papers published between 1969 and 2012. A summary of the study descriptive characteristics can be found in Table 1.

**Risk of Bias Within Studies**

The reported methodological quality of the included studies ranged between low and high risk of bias following QUIPS domains. Studies selected have shown to be heterogeneous considering bias, 7
presented high\textsuperscript{11,31,32, 36,37,41,43} risk of bias, 4 moderate\textsuperscript{34,38,39,42} and 5 low\textsuperscript{10,30,33,35,40} None of them fulfill all the methodological criteria. Summarized assessment considering risk of bias can be found in Table 2. Detailed results on the use of QUIPS\textsuperscript{26} tool in selected studies can be found in Supplemental Appendix 3.

Results of Individual Studies

There were 2 studies that investigated exclusively local modifications\textsuperscript{30,36} Other studies evaluated, besides general problems, local disturbances that could be involved on primary tooth eruption\textsuperscript{32,35,37,41} Hulland et al\textsuperscript{30} observed that 85\% of 128 teeth in 21 children presented gingival hyperemia in the early stages of eruption. Chakraborty et al\textsuperscript{36} reported that anterior teeth erupted with fewer local signs than posterior. King et al\textsuperscript{43} suggested that local signs could be confound with oral herpetic infection.

Shapira et al\textsuperscript{40} observed an increase in inflammatory cytokine levels in the gingival crevicular fluid surrounding erupting teeth, whereas Galili et al\textsuperscript{39} found that multiple eruptions occurring at the same time were associated with diseases. Bengtson et al,\textsuperscript{31} Carpenter,\textsuperscript{42} Cunha et al,\textsuperscript{32} and Yam et al\textsuperscript{41} observed that eruption of primary teeth was associated with symptoms. Kiran et al,\textsuperscript{37} Noor-Mohammed and Basha,\textsuperscript{38} and Peretz et al\textsuperscript{34} found more symptoms associated with the eruption of the incisors. Tasanen\textsuperscript{35} evaluated that mild symptoms like sucking fingers, rubbing gums, and drooling increased during teething, whereas Wake et al\textsuperscript{10} reported that primary tooth eruption was not associated with symptoms. Jaber et al\textsuperscript{11} found that tooth eruption in children was associated with fever and Ramos-Jorge et al\textsuperscript{33} found that there was a slight rise in body temperature.

The frequency of body temperature measurement varied between studies. In some of them daily registration could be assessed\textsuperscript{11,31,33,35,39} whereas in others every week day\textsuperscript{10} twice a week,\textsuperscript{40} or monthly.\textsuperscript{42} From the studies in which type of thermometer and measurement were informed, 4 studies used rectal temperature\textsuperscript{11,35,39,42} and 2 tympanic.\textsuperscript{10,33} In studies that presented these data, the cutoff point to consider a child with high temperature ranged from 37.5°C over a period of 2 days (rectal)\textsuperscript{39} to 39°C in a single assessment (not informed).\textsuperscript{34} A summary of body temperature assessment can be found in Table 3.

In relation to individual signs and symptoms, some investigations demonstrated that fever,\textsuperscript{11,31,32, 34,37–42} drooling,\textsuperscript{31,33–35,37,38,41,42} diarrhea,\textsuperscript{31–34,37,38,41,42} irritability,\textsuperscript{31–33,37,40,42} loss of appetite,\textsuperscript{31,33,35,37,42} sleeping problems,\textsuperscript{31–33,35,37} and rhinorrhea\textsuperscript{31–33,37,42} were associated with primary teeth eruption. In the opposite site, other studies exposed that the same symptoms (fever\textsuperscript{10,35} irritability\textsuperscript{10} sleep disturbances\textsuperscript{10,39} and loose stools\textsuperscript{10,39}) had no association with the eruption.

Synthesis of Results

To easily interpret the results, the studies were clustered into overall
<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bengtson et al 1988 Brazil&lt;sup&gt;21&lt;/sup&gt;</td>
<td>Institutionalized children living in a shelter</td>
<td>MTNED/ MTED (°C)</td>
</tr>
<tr>
<td>Carpenter 1978, United States&lt;sup&gt;46&lt;/sup&gt;</td>
<td>Well-infant clinic of a medical university hospital (South Carolina)</td>
<td>N</td>
</tr>
<tr>
<td>Chakraborty et al 1994, India&lt;sup&gt;56&lt;/sup&gt;</td>
<td>Pediatric departments of different hospitals of Calcutta and pedodontic department Dr. R. Ahmed Dental College</td>
<td>NI</td>
</tr>
<tr>
<td>Study Author, Year, Country</td>
<td>Study Design</td>
<td>Setting</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-------------</td>
<td>---------</td>
</tr>
<tr>
<td>Cunha, et al 2004, Brazil</td>
<td>RS</td>
<td>Infant clinic of Araçatuba Dental School</td>
</tr>
<tr>
<td>Galili et al 1969, Israel</td>
<td>PS</td>
<td>Institutionalized children residents of a Wizo Baby Home, Jerusalem</td>
</tr>
<tr>
<td>Study</td>
<td>Population</td>
<td>Intervention</td>
</tr>
<tr>
<td>-------</td>
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<td>--------------</td>
</tr>
<tr>
<td></td>
<td>Author, Year, Country</td>
<td>Study Design</td>
</tr>
<tr>
<td>Hulland et al 2000, Australia</td>
<td>PS</td>
<td>3 day care centers</td>
</tr>
<tr>
<td>Jaber et al 1992, Israel</td>
<td>PS</td>
<td>Author's private clinic to confirm tooth eruption</td>
</tr>
</tbody>
</table>

Infants cut their teeth with fever.
<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author, Year, Country</td>
<td>Study Design</td>
<td>Setting</td>
<td>Total n</td>
</tr>
<tr>
<td>King et al 1999, United States</td>
<td>CS</td>
<td>SG patient at a dental school pediatric dentistry clinic, a community hospital, and the private offices of a pediatric dentist and a pediatrician</td>
<td>40 Total</td>
</tr>
<tr>
<td>Kiran et al 2011, India</td>
<td>PS</td>
<td>Department of Pediatric and Preventive Dentistry, Institute of Dental Sciences, and the Department of Pediatrics, Rohilkhand Medical College</td>
<td>894</td>
</tr>
</tbody>
</table>
### TABLE 1 Continued

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Author, Year, Country</strong></td>
<td><strong>Study Design</strong></td>
<td><strong>Setting</strong></td>
<td><strong>Total n</strong></td>
</tr>
<tr>
<td>Noor-Mohammed and Basha 2012, India</td>
<td>CS</td>
<td>Child health institute and research center</td>
<td>1100</td>
</tr>
<tr>
<td>Peretz et al 2003, Colombia</td>
<td>CS</td>
<td>Public child center</td>
<td>585</td>
</tr>
</tbody>
</table>
TABLE 1 Continued

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Intervention</th>
<th>Questionnaire</th>
<th>Assessed Teeth</th>
<th>Symptoms</th>
<th>Follow-Up Period</th>
<th>MTNED/MTED °C</th>
<th>Main Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ramos-Jorge et al 2011, Brazil</td>
<td>PS/RS Residences of the infants</td>
<td>47, 5–15</td>
<td>11 validated trained dentists/daily</td>
<td>Mean 8.9 (± 2.7)</td>
<td>The day of eruption was defined as the first day on which the incisor edge emerged in the oral cavity without being completely covered by gingival tissue.</td>
<td>Tympanic 36.39 (0.26)</td>
<td>8 mo</td>
<td>There are associations between teething and sleep disturbance, increased salivation, rash, runny nose, diarrhea, loss of appetite, irritability, and a slight rise in temperature. Fever was more frequently reported in the RS.</td>
</tr>
<tr>
<td></td>
<td>Noninstitutionalized</td>
<td>Mean 8.9 (± 2.7)</td>
<td>Infrared auricular thermometer and a digital axillary thermometer.</td>
<td>251</td>
<td>The associations between signs and symptoms reported by mothers and tooth eruption were statistically significant.</td>
<td>Axillary 35.98 (0.36) MTED Tympanic 36.51 (0.20) Axillary 35.99 (0.46)</td>
<td></td>
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</tbody>
</table>

The most common symptoms on days of eruption were irritability, increased salivation, runny nose, and loss of appetite. Fever was reported % times more often in the RS.
<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shapira et al. 2003, Israel40</td>
<td>Pediatric dentist/Day care center 16 5–14</td>
<td>Information provided by parents/caregivers. Twice weekly.</td>
<td>MTNED During the control period, behavioral problems were observed in 50% of the children, compared to 16% in the control period (P &lt; .01). Fever was observed in 24% of the infants during tooth eruption and in 8% of the infants during the control period (P = .04). Coughing was observed in 12% during tooth eruption compared with 2% (P = .00) of the infants during the control period. In teething period vomiting (2%), drooling (12%), and appetite disturbances (12%), but were absence during the control period.</td>
</tr>
<tr>
<td></td>
<td>MTNED</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>MTED</td>
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</table>

MTNED/ MTED: Mean temperature normalized over day/ evening temperature difference; MTNED: mean temperature during teething period; MTED: mean temperature during the control period; NI: not indicated; MDT NI: mean difference temperature not indicated; P: probability. |
<table>
<thead>
<tr>
<th>Study</th>
<th>Author, Year, Country</th>
<th>Study Design</th>
<th>Setting</th>
<th>Total n</th>
<th>Age, Mean or Range, mo</th>
<th>Clinical Assessment</th>
<th>Body Temperature °C (Who/How)</th>
<th>Questionnaire</th>
<th>Assessed Teeth</th>
<th>Symptoms</th>
<th>Follow-Up Period</th>
<th>MTNED/MTED °C</th>
<th>Main Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wake et al 2000, Australia</td>
<td>PS/RS 3 child care centers 21</td>
<td>6 – 24 Mean 14.4 (+ 4.9)</td>
<td>Dental therapist examined for tooth eruption every weekday (midmorning) An eruption day was defined as the first day that the edge of an incisor or cusp of a molar crown could be seen or felt emerging through the gum.</td>
<td>Dental therapist every weekday (midmorning) Infrared tympanic thermometer</td>
<td>Two questionnaires to staff (afternoon) and parents (morning) Inquired about the child’s mood, wellness/illness, drooling/dribbling, sleep, stool, wet diapers, and rash/flushing over the preceding 24 h were answered every weekday. At the end of the study, parents completed a questionnaire about their beliefs and experiences related to teething.</td>
<td>90 (incisive, canine, molar).</td>
<td>Analysis did not indicate a relationship between tooth eruption and fever. All parents retrospectively reported that their own child had suffered teething symptoms.</td>
<td>7 mo MTNED 36.18</td>
<td>MTED 36.21</td>
<td>Tooth eruption is not associated with fever, mood disturbance, illness, sleep disturbance, drooling, diarrhea, strong urine, red cheeks, or rashes/flushing on the face or body.</td>
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</tr>
<tr>
<td>Yam et al 2002, Senegal</td>
<td>PS Child health institute Centre de Protection Maternelle et Infante in Dakar-Médina</td>
<td>499</td>
<td>5–30</td>
<td>Medical service Monthly. Mothers should bring the children if there were any signs or symptoms in this period.</td>
<td>Information provided by parents Type of thermometer, measurement NI</td>
<td>NI Number of teeth NI. Incisors, canines, and molars.</td>
<td>Local observation: 7 hematoma of eruption, 5 widespread gingivitis, 297 local gingivitis. At least 60% of the children had ≥1 of the symptoms: hyperthermia, vomiting, diarrhea and appetite problems.</td>
<td>NI</td>
<td>NI/NI</td>
<td>Children cut their teeth with local and systemic disturbances.</td>
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</table>
prevalence of signs and symptoms (Fig 2) and separately prevalence for each individual sign or symptom (Fig 3). A total of 10 studies were included in the meta-analysis. Eight studies had data enough to conduct the weighted average because data were insufficient. MTED, Mean temperature in eruption days; MTNED, Mean temperature in noneruption days.

It was not possible to calculate the weighted average because data were insufficient. MTED, Mean temperature in eruption days; MTNED, Mean temperature in noneruption days.

### TABLE 2 Risk of Bias Summarized Assessment (QUIPS26)

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</tr>
</thead>
<tbody>
<tr>
<td>Study participation</td>
<td>High</td>
<td>Mod</td>
<td>Low</td>
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<td>Low</td>
<td>Low</td>
<td>Low</td>
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<tr>
<td>Study attrition</td>
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<td>Mod</td>
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<td>High</td>
<td>X</td>
<td>Low</td>
<td>Low</td>
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<td>Mod</td>
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<tr>
<td>Outcome study confounding</td>
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<tr>
<td>Statistical analysis and presentation</td>
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<td>High</td>
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<tr>
<td>Overall</td>
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<td>High</td>
<td>Mod</td>
<td>Low</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>Mod</td>
<td>Mod</td>
<td>Low</td>
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</table>

Ratings: High, moderate, and low indicates high, moderate, and low risk of bias, respectively. PF, prognostic factor.

### FIGURE 2

Forest plot for all signs and symptoms that occurred during the eruption of primary teeth. Sample = 3506.

### FIGURE 3

Pooled prevalence for each individual sign or symptom that occurred during the eruption of primary teeth.

<table>
<thead>
<tr>
<th>Sign/Symptom</th>
<th>Pooled Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gingival Irritation</td>
<td>60</td>
</tr>
<tr>
<td>Irritability</td>
<td>80</td>
</tr>
<tr>
<td>Drooling</td>
<td>40</td>
</tr>
<tr>
<td>Snacking Sugar</td>
<td>20</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>30</td>
</tr>
<tr>
<td>Appetite Loss</td>
<td>20</td>
</tr>
<tr>
<td>Running nose</td>
<td>10</td>
</tr>
<tr>
<td>Fever</td>
<td>40</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>60</td>
</tr>
<tr>
<td>Fatty Rash</td>
<td>20</td>
</tr>
<tr>
<td>Vomiting</td>
<td>30</td>
</tr>
</tbody>
</table>

Prevalence of signs and symptoms (Fig 2) and separately prevalence for each individual sign or symptom (Fig 3). A total of 10 studies were included in the meta-analysis. Eight studies had data enough to conduct the weighted average because data were insufficient. MTED, Mean temperature in eruption days; MTNED, Mean temperature in noneruption days.
meta-analysis of general prevalence of signs and symptoms. Another 2 studies were included in the meta-analysis of individual signs or symptoms.33,35

Because of the heterogeneity between the studies, a random model was chosen.44 All the information about the meta-analysis of individual studies is described in Fig 2 and Supplemental Appendix 4. The results from this meta-analysis revealed that the overall prevalence of signs and symptoms associated with primary tooth eruption in children between 0 and 36 months was 70.5% (total sample = 3506; Fig 2), where gingival irritation, irritability, and drooling were the most frequent ones with 86.81%, 68.19%, and 55.72%, respectively. Additional information regarding the meta-analysis can be found in Supplemental Appendices 4 and 5.

**Risk of Bias Across Studies**

The studies were heterogeneous and had different designs. Analysis revealed that the weakness in methods was not considered an important confounder capable of masking possible signs and symptoms related to other diseases that could occur simultaneously with primary tooth eruption.

**DISCUSSION**

This systematic review investigated the available evidence about primary tooth eruption and local and systemic signs and symptoms. Currently, the American Academy of Pediatric Dentistry guidelines have indications that eruption of primary teeth leads to local discomfort, irritation, and drooling.45

Parents follow the development of children and witness any change in behavior, mood, or health. Thus, they can be helpful in assisting in the detection of related problems.46 Although cooperative, parents retrospectively reported symptoms associated with primary tooth eruption were memory biased. In a retrospective study about parents’ beliefs related to primary tooth eruption, the mean number of symptoms reported per child was 11, whereas in the study sample the mean number was 8.10 Similarly, fever was reported 5 times more often in the retrospective than children experienced fever during teething period in the prospective study.33 Limitations of these studies are represented by the subjectivity of the parents’ observations. In this context, a study that had the collaboration of parents who daily measured children’s temperature, checked for tooth eruption, and kept a daily log of symptoms, despite presented adequate methods, was excluded based on the criteria for this systematic review because children did not receive health professional examination during the follow-up. There was a significant association to tooth emergence: biting, drooling, gum rubbing, irritability, sucking, sleep awakenings, ear rubbing, rash on face, decreased appetite for solids, and slight temperature elevation.6

Regarding the local signs, the most frequent was inflammation of the gum36 or gingival reddening (hyperemia),30 mostly in posterior teeth. The timing of eruption of the primary teeth (6 months onward) coincides with the age when infants start to explore the environment. In this phase, the introduction of the hands and objects into the mouth is normal; this, in turn, can bring harmful microorganisms and cause infection.47 Even sucking behavior, nutritive and nonnutritive, may lead to bruising or may traumatize the gums causing inflammation.48

Regarding the most frequent general symptoms during primary tooth eruption, irritability and drooling were the most observed followed by decreased appetite, sleeping problems, rhinorrhea, fever, diarrhea, rash, and vomiting. Eruption was associated with fever,60 did not influence the body temperature,35 or leads to a slight rise in body temperature.33 In contrast, symptoms that were not related to primary tooth eruption in the selected studies were in this sequence: sickness,10,35,39 sleeping disturbances,10,39 loose stools,10,39 drooling,10,39 vomiting,39 and fever.10,35 Three of most robust studies in this systematic review showed that sucking fingers, gum rubbing, daytime restlessness, loss of appetite,75 sleep disturbance, increased salivation, rash, rhinorrhea, diarrhea, irritability,33 and coughing40 increased during teething.

Another robust study,10 which accompanied 90 erupting teeth from 21 children every weekday, reported that fever, mood disturbance, illness, sleeping disturbance, drooling, diarrhea, strong urine, red checks, or rashes did not have association with primary tooth eruption.

The stage of eruption considered to represent the day of eruption for the studies differed from the first day the edge of an incisor or a cusp of a molar could be seen or felt emerging through the gum,10,33 palpable with the fingernail35; clinical crown of the tooth visible but not exceeding 3 mm or leads to a slight rise in body temperature,335 in the gingiva but not exceeding 3 mm or to any portion of the occlusal surface penetrated the gingiva.39 Besides that, the frequency of clinical examination varied from single in cross-sectional (CS) studies to daily assessment in some prospective investigations. This is important information, as Hulland et al30 found that the mean duration of primary tooth eruption from imminent eruption to completion of the emergence phase was in an average rate of 0.7 mm per month. Those studies that evaluated the eruption as the tooth crown visible through gingiva but not exceeding 3 mm or those in which clinical examinations...
occurred in monthly intervals may have lost or overestimated some signs or symptoms.

It seems that symptoms associated with primary tooth eruption decrease with age. Most manifestations were observed during the eruption of primary incisors or were studied only in incisors. Also there was a significant difference between the mean age at which eruptions were accompanied by disturbances (11.8 months) and the average age (14.8 months) at which teeth erupted without general disturbances. On the other hand, there seems to be an association between multiple eruption with fever and respiratory and alimentary illnesses that could be due to the stress that led to the low resistance of the body against infections.

Accurate determination of body temperature is essential to diagnose fever. A recent systematic review investigating the accuracy of infrared tympanic thermometry used in the diagnosis of fever in children, disclosed that the accuracy of this kind of thermometer is high, using rectal measurement as the “gold standard.” Besides, as temperature measured by tympanic thermometry was always 0.6°C to 0.2°C less than rectal temperature, the threshold of fever diagnosed by tympanic thermometry can be decreased. Therefore, if 38.0°C is the fever diagnosed by rectal temperature, the threshold of infrared tympanic thermometry should be 37.4°C to 37.8°C. Under these circumstances, in this systematic review, in 1 study using rectal temperature, mothers on a daily basis verified temperature and the threshold point was not informed. Fever was associated with teething and the mean daily temperature in days of noneruption was between 36.90°C and 37.10°C, and on the eruption day 37.60°C. Two studies with moderate risk of bias used rectal temperatures >37.77°C (100°F) and >37.50°C; these authors stated that fever was associated with tooth eruption, but mean daily temperature was not informed. Analyzing the 3 most robust studies, 1 used rectal temperature and detected that eruption did not interfere in body temperature with mean daily temperature in noninfected children (37.0°C in noneruption days and 36.9°C in eruption days) in twice-daily examinations. The others used tympanic measurements. One study discovered a slight rise from 36.39°C in noneruption days to 36.51°C in eruption days in a daily check by dentists, whereas the other stated that children do not have fever during the teething period, with 36.18°C in noneruption days and 36.21°C in eruption days every weekday by the dental therapist.

LIMITATIONS

Some methodological limitations of this review should be considered. Different general symptoms were considered among studies and not all studies related confounding factors, such as other disease that might have occurred with tooth eruption, or several symptoms happening at the same time. All of these may obscure the actual findings.

Most studies failed to expose a clear definition of the diagnostic methods. Examinations were performed in long intervals that could compromise adequate data collection. Besides, some symptoms did not use objective measures, but parents’ observation, such as irritability and loss of appetite. In addition, some symptoms need more specific examination, such as diarrhea that may be caused by infection and, without a virology study the diagnostic is not conclusive.

Most of the selected studies demonstrated a high risk of bias, especially in relation to study design. Articles with lower risk of bias had small samples: 21 to 126 children evaluated. The biggest samples were found in studies with high risk of bias, although a random effect for meta-analysis was used, this might have affected the results.

CONCLUSIONS

Based on the current limited evidence, there are signs and symptoms during primary tooth eruption. Gingival irritation, irritability, and drooling were the most common. For body temperature analyses, it was possible to evaluate that eruption of primary teeth is associated with a rise in temperature, but it was not characterized as fever.

ABBREVIATIONS

CG: control group
CI: confidence interval
CS: cross-sectional
LILACS: Latin American and Caribbean Health Sciences
QUIPS: Quality in Prognosis Studies Tool
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Pediatrics; originally published online February 18, 2016;
DOI: 10.1542/peds.2015-3501

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