Treatment of Ankyloglossia and Breastfeeding Outcomes: A Systematic Review

David O. Francis, MD, MSa, Shanthi Krishnaswami, MBBS, MPHb, Melissa McPheeters, PhD, MPHb,c

OBJECTIVE: Ankyloglossia is a congenital condition characterized by an abnormally short, thickened, or tight lingual frenulum that restricts tongue mobility. The objective of this study was to systematically review literature on surgical and nonsurgical treatments for infants with ankyloglossia.

METHODS: Medline, PsycINFO, Cumulative Index of Nursing and Allied Health Literature, and Embase were searched up to August 2014. Two reviewers independently assessed studies against predetermined inclusion/exclusion criteria. Two reviewers independently extracted data regarding participant and intervention characteristics and outcomes and assigned quality and strength-of-evidence ratings.

RESULTS: Twenty-nine studies reported breastfeeding effectiveness outcomes (5 randomized controlled trials [RCTs], 1 retrospective cohort, and 23 case series). Four RCTs reported improvements in breastfeeding efficacy by using either maternally reported or observer ratings, whereas 2 RCTs found no improvement with observer ratings. Although mothers consistently reported improved effectiveness after frenotomy, outcome measures were heterogeneous and short-term. Based on current literature, the strength of the evidence (confidence in the estimate of effect) for this issue is low. We included comparative studies published in English. The evidence base is limited, consisting of small studies, short-term outcomes, and little information to characterize participants adequately. No studies addressed nonsurgical interventions, longer-term breastfeeding or growth outcomes, or surgical intervention compared with other approaches to improve breastfeeding, such as lactation consultation.

CONCLUSIONS: A small body of evidence suggests that frenotomy may be associated with mother-reported improvements in breastfeeding, and potentially in nipple pain, but with small, short-term studies with inconsistent methodology, strength of the evidence is low to insufficient.
Ankyloglossia is a congenital condition characterized by an abnormally short, thickened, or tight lingual frenulum that restricts mobility of the tongue. It is typically an isolated anomaly, but can be associated with other craniofacial abnormalities. It variably causes reduced tongue mobility and has been associated with functional limitations in breastfeeding, swallowing, articulation, orthodontic problems including malocclusion, open bite, separation of lower incisors, mechanical problems related to oral clearance, and psychological stress. Estimates range from 2.1% to 10.7%, but definitive incidence and prevalence statistics are elusive because of an absence of a criterion standard or clinically practical diagnostic criteria. This article focuses specifically on treatment of ankyloglossia in the presence of breastfeeding difficulties, with the goal of improving breastfeeding outcomes.

Recognition of potential benefits of breastfeeding in recent years has resulted in a renewed interest in functional ankyloglossia sequelae. Of infants with ankyloglossia, there is a reported 25% to 80% incidence of breastfeeding difficulties, including failure to thrive, maternal nipple damage, maternal breast pain, poor milk supply, maternal breast engorgement, and refusing the breast. Ineffective latch is hypothesized to underlie these problems. Mechanistically, infants with restrictive ankyloglossia cannot extend their tongues over the lower gum line to form a proper seal and therefore use their jaws to keep the breast in the mouth. Adequate tongue mobility is required, and infants with ankyloglossia often cannot overcome their deficiency with conservative measures such as positioning and latching techniques, thereby requiring surgical correction. Despite these studies, consensus on the role of ankyloglossia in breastfeeding difficulties is lacking. A minority of surveyed pediatricians (10%) and otolaryngologists (30%) believe ankyloglossia commonly affects feeding, whereas 69% of lactation consultants feel that it frequently causes breastfeeding problems. Therefore, depending on the audience, enthusiasm for its treatment varies. Currently, the National Health Service and the Canadian Pediatric Society recommend treatment if ankyloglossia interferes with breastfeeding. However, a standard definition of “interference” with breastfeeding is not provided, leaving room for interpretation and variation in treatment thresholds. Lack of data on the natural history of untreated ankyloglossia further promulgates uncertainty. Some propose that a short frenulum elongates spontaneously due to progressive stretching and thinning of the frenulum with age and use. However, there are no prospective longitudinal data on the fate of the congenitally short lingual frenulum. Without this information, it is difficult to inform parents fully about the long-term implications of ankyloglossia, thereby complicating the decision-making process.

This review describes outcomes reported in studies identified for a broader Agency for Healthcare Research and Quality (AHRQ)-commissioned systematic review of interventions for infants and children with congenital ankyloglossia. The aim of this article was to investigate the benefits of surgical treatment of newborns and infants who are born with ankyloglossia and who present with breastfeeding difficulties. The full review and its protocol are available at http://www.effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=1991.

METHODS

Search Strategy
We searched Medline via the PubMed interface, the Cumulative Index of Nursing and Allied Health Literature, Embase (Excerpta Medica Database), and PsycINFO (psychology and psychiatry literature), with no publication date restrictions by using relevant vocabulary terms and key terms related to ankyloglossia and its therapies. Reference lists of all included articles and recent reviews related to ankyloglossia therapies were hand-searched to identify any additional potentially relevant articles.

Study Selection
Inclusion and exclusion criteria were developed in consultation with an international expert panel of clinicians and researchers who treat and study ankyloglossia. Treatment effectiveness data were extracted from comparative study designs (ie, randomized controlled trials [RCT], nonrandomized trials, prospective or retrospective cohort studies). Harms data were collected comprehensively from all study types including case series and case reports. Each study was reviewed independently by 2 investigators against inclusion criteria (Table 1) with disagreements resolved through adjudication by a senior investigator.

Data Extraction
Two investigators independently extracted data regarding study design; descriptions of the study populations, interventions, and comparison groups; and baseline and outcomes data (including harms/adverse events) by using standardized forms. Principal outcomes of interest were latch effectiveness, maternally reported nipple pain associated with breastfeeding, breastfeeding effectiveness, and duration.

Study Quality Assessment
Two team members independently conducted quality assessment of each study by using forms developed by the review team with input from content experts. Discrepancies were
TABLE 1 Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
<th>Category</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study population</td>
<td>Inclusion: Children ages 0–18 with ankyloglossia or ankyloglossia with concomitant tight labial frenulum (lip-tie); Exclusion: Studies with participants with Van der Woude syndrome, Pierre Robin syndrome, Down syndrome, or craniofacial abnormalities were excluded, as were studies of premature infants (&lt;37 wk of gestation)</td>
</tr>
<tr>
<td>Publication languages</td>
<td>Inclusion: English Exclusion: Non-English</td>
</tr>
<tr>
<td>Admissible evidence (study design and other criteria)</td>
<td>RCTs, prospective and retrospective cohort studies, nonrandomized controlled trials, prospective and retrospective case series, and crossover studies Case reports to assess harms Other criteria: Original research studies providing sufficient detail regarding methods and results to enable use and aggregation of the data and results Studies must address 1 or more of the following:  • Surgical interventions (simple anterior frenectomy, laser frenulectomy, posterior frenulectomy, Z-plasty repair)  • Nonsurgical treatments include complementary and alternative medicine (CAM) therapies (eg, craniosacral therapy, myofascial release, and other chiropractic therapies), lactation intervention, speech therapy, physical therapy, oral motor therapy, and stretching exercises/therapy  • Baseline and outcome data (including harms) related to interventions for ankyloglossia Relevant outcomes must be able to be extracted from data in the papers Data must be presented in the aggregate (versus individual participant data)</td>
</tr>
</tbody>
</table>

Adjudicated through discussion between the assessors to reach consensus or via a senior reviewer. Investigators did not rely on the study design as described by authors of individual articles; rather, the methods section of each article was reviewed to determine which rating tool to use. The results of these tools were then translated to the AHRQ quality designation standards of “good,” “fair,” and “poor.”

Strength of evidence of current research was assessed by using methods established in the AHRQ Effective Health Care Program’s Methods Guide for Effectiveness and Comparative Effectiveness Reviews. Assessments were based on 5 domains: study limitations, consistency in direction of effect, directness in measuring intended outcomes, precision of effect, and reporting bias. (Table 2). Strength of evidence was determined for major intervention-outcome pairs by using a prespecified approach described in the full review.

Data Synthesis
Considerable heterogeneity of study design and outcome measures of studies meeting inclusion criteria obviated the ability to perform any meta-analyses. Therefore, characteristics of the study populations and interventions were summarized and descriptive statistics used to report study outcomes.

RESULTS
Figure 1 shows the flow of articles retrieved. In all, 29 studies addressed the benefits of surgical treatment intended to improve breastfeeding outcomes; there were no studies of nonsurgical treatments. There were 5 RCTs (Tables 3 and 4), which were rated good,7–9 fair,10 and poor11 quality for outcomes related to breastfeeding effectiveness and maternal pain related to breastfeeding. One poor-quality retrospective cohort12 and 23 case series,13–35 also addressed outcomes of surgical treatment. Table 5 outlines breastfeeding effectiveness measures used in these studies. The focus of this review was on the RCTs of higher quality, but we note that lower-quality studies typically reported improvements in breastfeeding effectiveness.

Two RCTs compared frenotomy to sham surgery,7,8 1 to usual care,9 1 to intensive lactation consultation,10 and 1 used a crossover design to compare frenotomy followed by sham surgery or sham surgery followed by frenotomy with assessment of breastfeeding after each order of intervention (ie, frenotomy or sham).11 The retrospective cohort study also compared frenotomy with usual care.12 For all studies, sham comparison involved taking the infant to the intervention room for the same amount of time as infants receiving the procedure and then returning the infant to the mother.

The earliest reported RCT used nonblinded maternally assessed breastfeeding effectiveness and reported that 96% of frenotomized infants had improved feeding within 48 hours compared with 3% in the control group, but this study had significant limitations (eg, lack of blinding, unclear randomization scheme, lack of data on longer-term follow-up, and crossover of 27/28 control subjects after 48-hour outcome assessment).10 In a second RCT, mothers again self-reported improved breastfeeding among infants immediately after frenotomy (78% in treated group versus 47% in comparison group, P < .02).8 Three RCTs used an observer to assess breastfeeding effectiveness,7–9
In all 3, the observer was blinded to the treatment. Among these, 1 reported improvement in breastfeeding effectiveness based on the Infant Breastfeeding Assessment Tool (IBFAT; score range = 0 [poor feeding] to 12 [vigorous and effective feeding]) score immediately after frenotomy compared with sham treatment (mean 11.6 ± 0.81 vs 8.07 ± 0.86, P = .026). In contrast, in 2 of the 3 RCTs, the independent blinded observers did not detect a difference in breastfeeding improvement.8,9

Outcomes that failed to show a difference in these 2 RCTs included percent improvement (50% vs 40%) immediately after intervention and LATCH (Latch, Audible swallowing, Type of nipple, Comfort, Hold) and IBFAT change 5 days postintervention (LATCH change score: median 1 [IQR 0–2] versus median 1 [IQR 0–2], P = .52 and IBFAT change score: 0 [IQR −1.8–1.0] vs 0 [IQR 0–1], P = .36). One RCT reported significant and immediate improvement in maternally reported nipple pain among frenotomized infants compared with sham treatment.7 Both remaining RCTs found nonsignificant reductions in maternally reported nipple pain between the frenotomy and sham groups at immediate and 5-day postprocedure assessments.8,9 However, in the 1 study that assessed pain at 5 days (the longest follow-up), a large number of mothers in the control group crossed over to receive frenotomy before outcomes were assessed.9

Harms
To identify all possible harms, we sought harms from all comparative studies and case series that were identified as potentially providing effectiveness data, and also reviewed case reports of harms. Forty-six studies reported that they looked for harms; either reporting actual harms or reporting that they found none. These included 5 RCTs,7–11 1 cohort study,12 25 case series,13,15,16,18–21,24–30,32,33,35–43 and 15 case reports.44–58 Most studies reporting harms information explicitly noted that no significant harms were observed (n = 17).7,9–11,13,15,18,20,24,25,28–30,35,36,41,43 or reported minimal harms. Among studies reporting harms, bleeding was most frequently reported.8,16,19,33,37 Bleeding was typically described as minor and limited, and would be expected with a minor surgical intervention. Few studies described what specific methods were used to collect harms data.

DISCUSSION
Management of congenital ankyloglossia is receiving increased attention, as it represents

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**TABLE 2** Strength of Evidence Grades and Definitions

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>We are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. We believe that the findings are stable (ie, another study would not change the conclusions).</td>
</tr>
<tr>
<td>Moderate</td>
<td>We are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains.</td>
</tr>
<tr>
<td>Low</td>
<td>We have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.</td>
</tr>
<tr>
<td>Insufficient</td>
<td>We have no evidence, we are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome. No evidence is available or the body of evidence has unacceptable deficiencies, precluding reaching a conclusion.</td>
</tr>
</tbody>
</table>

Excerpted from Berkman et al.9

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In all 3, the observer was blinded to the treatment. Among these, 1 reported improvement in breastfeeding effectiveness based on the Infant Breastfeeding Assessment Tool (IBFAT; score range = 0 [poor feeding] to 12 [vigorous and effective feeding]) score immediately after frenotomy compared with sham treatment (mean 11.6 ± 0.81 vs 8.07 ± 0.86, P = .026). In contrast, in 2 of the 3 RCTs, the independent blinded observers did not detect a difference in breastfeeding improvement.8,9

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**FIGURE 1** Disposition of articles identified by the search strategy. aIncludes data from 1 unpublished thesis. bNumbers do not tally, as studies could be excluded for multiple reasons.
a potentially actionable impediment to effective breastfeeding. The trend toward breastfeeding has been promulgated based on its demonstrated health benefits to the infant. It is proposed that anterior tethering of the tongue related to ankyloglossia reduces the effectiveness of latch to the breast, disrupts efficient milk transfer, and increases maternal discomfort during breastfeeding. Therefore, many advocate ankyloglossia release (eg, frenotomy) to prevent breastfeeding difficulties or to improve breastfeeding effectiveness. This systematic review evaluated the comparative effectiveness of ankyloglossia treatment at improving breastfeeding outcomes.

Overall, the strength of evidence on this topic is low for improving breastfeeding and reducing maternal nipple pain and insufficient to assess the effect of frenotomy on length of breastfeeding based on small studies and heterogeneous methodology, meaning that future research could change our understanding of the estimate of effect. Nonetheless, synthesis of study results demonstrated a few important findings. In all, 5 comparative studies were identified, which variably defined ankyloglossia and outcomes used to measure the effectiveness of its treatment on breastfeeding results. Studies in the remainder in the literature base were case series, thus providing no comparative effectiveness data. Therefore, meta-analysis of results was not possible.

Included in the analysis were 3 good-quality RCTs,7–9 and 1 fair-quality RCT.10 The good-quality RCTs were relatively consistent in demonstrating improvement in breastfeeding effectiveness immediately or within 5 days of frenotomy compared with sham or no intervention, respectively.7–9 These same studies had disparate findings with regard to whether frenotomy decreased maternal nipple pain. Only the RCT performed on infants at 6 days of age showed a significant reduction in maternal pain.7 Those performed on infants a few weeks older did not

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**TABLE 3  Breastfeeding Effectiveness After Surgical Procedures (RCTs)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Age, d (IQR, Range, Mean, or Mean ± SD)</th>
<th>Baseline Measures</th>
<th>Outcomes at 5 d</th>
<th>Outcomes at 8 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>LATCH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emond et al 20139</td>
<td>Mean at 5 d follow-up (IQR)</td>
<td>G1+G2: ≤ 8</td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
</tr>
<tr>
<td>G1: Frenotomy, 55/52</td>
<td>G1: 11 (8–14)</td>
<td>G1: 9 (8–10)</td>
<td>G1: 10 (10–10)</td>
<td></td>
</tr>
<tr>
<td>Quality: Good</td>
<td>G1 vs. G2: P = .10</td>
<td>G1 vs. G2: P = .41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dollberg et al 200611</td>
<td>Range of days</td>
<td>Mean ± SD.</td>
<td>Mean ± SD.</td>
<td>NA</td>
</tr>
<tr>
<td>G1: Frenotomy, breastfeeding/ sham, breastfeeding, 15/14</td>
<td>G1+G2: 1–21</td>
<td>G1+G2: 6.4±2.3</td>
<td>G1+ G2: 6.8±2.0</td>
<td>P = .06 compared with baseline</td>
</tr>
<tr>
<td>G2: Sham, breastfeeding, frenotomy, breastfeeding, 11/11</td>
<td>Quality: Poor</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BSES-SF

<table>
<thead>
<tr>
<th>Study</th>
<th>Age, d (IQR, Range, Mean, or Mean ± SD)</th>
<th>Baseline Measures</th>
<th>Outcomes at 5 d</th>
<th>Outcomes at 8 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emond et al 20139</td>
<td>Mean at 5 d follow-up (IQR)</td>
<td>NR</td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
</tr>
</tbody>
</table>

IBFAT

<table>
<thead>
<tr>
<th>Study</th>
<th>Age, d (IQR, Range, Mean, or Mean ± SD)</th>
<th>Baseline Measures</th>
<th>Outcomes at 5 d</th>
<th>Outcomes at 8 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emond et al 20139</td>
<td>Mean at 5 d follow-up (IQR)</td>
<td>NR</td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
</tr>
<tr>
<td>G1: Frenotomy, 55/52</td>
<td>G1: 11 (8–14)</td>
<td>G1: 12 (11–12)</td>
<td>G1: 12 (12–12)</td>
<td></td>
</tr>
<tr>
<td>Quality: Good</td>
<td>G1 vs. G2: P = .76</td>
<td>G1 vs G2: P = .58</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Buryk et al 20117 | Mean days ± SD at | IBFAT, mean ± SE. | Immediately after | NA |
| procedure, mean ± SE. | G1: 6.2 ± 6.9 | G1: 9.3 ± 0.89 | G1: 11.8 ± 0.81 |
| G1: Frenotomy, 30 | G2: 6.0 ± 7.0 | G2: 8.5 ± 0.73 | G2: 8.07 ± 0.86 |
| G2: Sham procedure, 28 | G1 vs G2: P = .029 | G1 vs G2: P = .29 |
| Quality: Good | Effect size: 0.31 |

Not all RCTs reported these measures. BSES-SF, Breastfeeding Self-Efficacy Scale-Short Form; G, group; NA, not applicable; NR, not reported.
report either an immediate\textsuperscript{8} or 5-day\textsuperscript{9} reduction in pain. The difference between early or later frenotomy on nipple pain may relate to cumulative trauma on the breast from several weeks with inefficient latch from tongue-tied infants.

### Limitations of Evidence Base

Besides variability in age at treatment, a number of other issues were identified. No study effectively assessed mid- and long-term outcomes of frenotomy. This is concerning because the goal of treatment is to optimize breastfeeding duration to maximize its purported health benefits to the infant, but longer-term comparative effects are unavailable. Although longer-term data exist in case series studies,\textsuperscript{59} lack of a control or comparison group limited the ability to determine whether the treatment or natural history affected the outcome. Thus, the determination was made that the strength of evidence for mid- and long-term outcomes was currently insufficient.

Finally, no comparative literature exists to assess the effectiveness of nonsurgical and conservative treatment of ankyloglossia. Not all patients identified with ankyloglossia may have difficulty breastfeeding and/or need surgery. However, no data exist to differentiate how these patients may fare later in life. Compounding this deficiency is a limited understanding of the natural history of ankyloglossia. More research is needed to characterize which tongue-tied infants need...
surgical intervention and whether it has the long-term positive benefits that have been promoted by advocates.

Applicability of Findings

Inclusion criteria were set to identify studies with applicability to newborns and infants with ankyloglossia. Studies differed in terms of study population and outcome measures. Most studies were noncomparative, and lack of direct comparisons of treatment options further hinders the ability to understand what findings will best extend to a specific newborn or infant or a decision about care protocols. Overall, the data that are available may be applicable to newborns with ankyloglossia with feeding problems. There is no evidence to suggest that the data would be applicable to infants with ankyloglossia who do not present with feeding problems.

Furthermore, in included studies, newborns referred for treatment of ankyloglossia were born primarily at tertiary care centers and recognized as having difficulty with breastfeeding concomitant with ankyloglossia. Most infants are not born at tertiary care centers; thus, extrapolation to other birthing sites may not be possible. Moreover, newborns of mothers not choosing to breastfeed may not be recognized or diagnosed, as breastfeeding difficulty is typically used as an indicator to evaluate for ankyloglossia. Interestingly, 2 studies reported that all patients had lactation consultation before enrollment without significant improvement in feeding. Arguably, this limits the applicability of their results to newborns who had and failed to improve adequately with such consultation.

In these studies, various clinicians were involved in making the ankyloglossia diagnoses; however, assessment of breastfeeding difficulty and diagnostic criteria for ankyloglossia were not universally described. Lack of a consistent objective measure to define and classify this condition may limit the reproducibility of findings. Furthermore, patients in these studies were between a median 6 days of age and up to a mean of 33 days of age (range 6–115) in another study. Applicability to findings in older infants cannot be gleaned from these data. Furthermore, durability of results cannot be assessed based on these findings.

Frenotomy was the only intervention used in the good-quality RCTs, although clinicians report that other interventions are being used in practice. Overall, the specifics of the procedure were inconsistently reported. As such, the extent of posterior extension of the incision was not clearly defined and appears to be left up to the clinical expertise of the proceduralist. Moreover, the comparators used were sham surgery and no intervention. These outcomes are identical except with regard to blinding and outcome assessment. “No intervention” is the primary alternative to frenotomy in the population and is therefore an appropriate comparator that is applicable to the broader population.

Study Limitations

This review included only studies published in English. Our scan and review of non-English references revealed a high percentage of noneligible items. Given the high percentage of noneligible items in this scan (97%), we feel that excluding non-English studies did not introduce significant bias into the review. The review focused on comparative studies (studies including an intervention and a comparison group). However, we did identify case series data to determine whether it could provide support for the comparative findings, and to identify potential harms of intervention.

Research Gaps

There are several important gaps in the current evidence base. First, there is an absence of comparative studies assessing effectiveness of nonsurgical treatments for ankyloglossia. Second, there is a need for a standardized approach to diagnosis/classification of ankyloglossia to improve comparability of outcomes. Third, the natural history of ankyloglossia through childhood is unknown; making it unclear which affected infants would most benefit from frenotomy or more conservative treatment. Fourth, little is understood about the role of age on effectiveness of frenotomy. Specifically, there appears to be variable outcomes based on whether the procedure is performed early or late in infancy. Finally, there is a paucity of data on the durability of outcomes after frenotomy. This is a critically important gap in the literature, particularly, because exclusivity of breastfeeding is currently being promoted for infant health and is the primary impetus for treating ankyloglossia.

CONCLUSIONS

A small body of evidence suggests that frenotomy may be associated with improvements in breastfeeding as reported by mothers, and potentially in nipple pain, but with small, short-term studies, inconsistently conducted, strength of evidence is generally low to insufficient. Research is lacking on nonsurgical interventions and on the differential mid- to long-term breastfeeding effectiveness outcomes among infants treated for ankyloglossia.

ACKNOWLEDGMENTS

Ms Tanya Surawicz contributed to the data collection and interpretation. Ms Annette Williams and Ms Nila Sathe designed the data collection instruments and coordinated and supervised data collection. Ms Katherine Worley assisted in the preparation of the manuscript.
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