Canadian Agency for Drugs and Technologies in Health

RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

TITLE: Frenectomy for the Correction of Ankyloglossia: A Review of Clinical Effectiveness and Guidelines

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CONTEXT AND POLICY ISSUES

The World Health Organization promotes breastfeeding as the primary source of nutrition during the first six months of life, followed by supplemental breastfeeding for an additional 2 years, or beyond, with appropriate complementary feeding.[1] Health Canada, the Canadian Paediatric Society, Dietitians of Canada, and the Breastfeeding Committee for Canada have issued a similar joint statement to this effect.[2] These recommendations are in the interest of promoting proper nutrition and immunologic protection, and to promote the growth and development of infants and toddlers. Perhaps in response, interest in the practice of breastfeeding has grown. Based on results from the Canadian Community Health Survey, 89% of mothers in Canada breastfed in 2011 to 2012, up from 85% in 2003.[3] Breastfeeding mothers who stopped before the six-month mark did so due to the perception that they had insufficient milk supply, difficulty with the breastfeeding technique, and medical conditions in the mother or child, among other reasons.[3]

One medical condition associated with breastfeeding problems is ankyloglossia, or tongue-tie, a congenital anomaly in which a child is born with an abnormally short and/or thick lingual frenulum that limits the movement of the tongue. It has been associated with difficulty breastfeeding due to trouble latching on, associated nipple pain, infection, and poor milk supply in mothers, as well as discontinuation of breastfeeding and inadequate weight gain and other health issues such as oral hygiene concerns, speech problems, and developmental and social consequences.[4] Ankyloglossia has a hereditary link, but not all cases are explained by genetics.[5] A review of studies reporting on prevalence of ankyloglossia in the United Kingdom and USA suggested that rates likely fall between 4 to 10%, occurring more commonly in males, though inconsistency in diagnostic procedures may contribute to variation in estimates.[6,7] There is no clinical standard for diagnosing ankyloglossia, but assessment tools such as the Hazelbaker Assessment Tool for Lingual Frenulum Function (HATLFF), which is considered comprehensive, but difficult to use,[8] and the Bristol Tongue Assessment Tool (BTAT),[9] which is simpler and aims to ease implementation, are cited in the literature. Diagnoses may also be made using subjective clinical judgement by practitioners with varying levels of experience or

expertise. The condition can entail mild immobility or be as severe as fusion of the entire tongue to the floor of the mouth.[10] The condition can be anterior or posterior, and may be comorbid with other issues such as upper lip-tie.[11-13]

To correct ankyloglossia, splitting of the tongue-tie, termed frenectomy (also commonly referred to as frenotomy or frenulotomy), is often proposed. It can be conducted using a laser, scalpel, or surgical scissors, and the laser procedure is suggested to be more accurate, and provide greater patient-perceived success, and hemostasis.[14] Frenuloplasty (also called Z-plasty) is a type of tongue-tie release often conducted with anesthetic in which more precise incisions and closure of the wound in a specific pattern occurs, with the aim of lengthening the anterior tongue. Simple release is a procedure in which the frenulum is detached without any wound closure or alteration, usually without anesthetic. Based on population data from British Columbia, the rate of frenotomy increased by 89% from 2004 to 2013, rising from 2.8 to 5.3 per 1000 live births.[15] This suggests a possible increased awareness, interest in frenotomy, and increase in diagnostic capacity.

There is disagreement across specialties regarding whether a tongue-tie should be divided to facilitate breastfeeding, and under what circumstances.[16] Ankyloglossia is not the only cause of breastfeeding issues, and in cases of comorbidities or alternative primary causes, frenectomy may not result in resolution. Un-split lingual frenulum may physically adapt (i.e., stretch with age) over time and breastfeeding quality may improve without intervention.[17] The Canadian Paediatric Society has communicated that under most circumstances, tongue-tie is an incidental anatomical finding without significant consequences for the quality of breastfeeding,[18] and that surgical intervention may not be warranted unless difficulty breastfeeding or other clinical concerns present themselves. The National Institute for Health and Care Excellence in the UK released guidance in 2005 which reported that current evidence was suggestive of no major safety concerns with frenectomy, and that there was limited evidence that it might improve breastfeeding.[10] Considering uncertainties regarding the clinical effectiveness and appropriateness of the procedure, and the development of new technologies and methods of conduct, this report aims to review the current clinical evidence regarding the effectiveness of frenectomy in newborns and infants with ankyloglossia, as well as evidence-based guideline recommendations for the use of this procedure.

RESEARCH QUESTIONS

1. What is the clinical effectiveness of frenectomy for the correction of ankyloglossia in newborns and infants?

2. What are the evidence-based guidelines regarding frenectomy for the correction of ankyloglossia in newborns and infants?

KEY FINDINGS

The clinical effectiveness of frenectomy for the correction of ankyloglossia in newborns and infants was addressed by two systematic reviews, one randomized controlled trial, and four non-randomized studies. No evidence-based guidelines were identified; however, three guidance documents are discussed within a systematic review. Overall, there is evidence that frenectomy is a safe procedure with demonstration of benefit for short-term breastfeeding effectiveness as perceived by the mother. There is less robust evidence, and thus, more uncertainty regarding objective and long-term measurements of breastfeeding effectiveness, reduction of maternal

breast and nipple pain and feeding problems, increased continuation and duration of breastfeeding, and proper growth. Quality concerns with the literature included subjective outcome measures, poor generalizability, potential confounding, and unclear reliability of pooled and poor quality data. Frenectomy may benefit children of mothers who wish to improve their perceived breastfeeding effectiveness, at least in the short-term. Accordingly, older guidance states that when appropriate and conducted by a qualified practitioner, frenectomy is safe and likely beneficial to the patient.

METHODS

Literature Search Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD), and CINAHL databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2011 and May 17, 2016.

Rapid Response reports are organized so that the evidence for each research question is presented separately.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Newborns and infants with ankyloglossia (tongue tie) for whom breastfeeding is not successful or is difficult
Intervention	Lingual frenectomy[a]
Comparator	Counselling by a lactation consultant; Any active comparator; No treatment
Outcomes	Q1: Clinical effectiveness (e.g., improvement in breastfeeding); Harms; Q2: Evidence-based guidelines regarding the appropriate indications and use of frenectomy for newborns and infants
Study Designs	Health technology assessments, systematic review, meta-analyses, randomized controlled trials, non-randomized studies, evidence-based guidelines

[a]also referred to as frenotomy, frenulectomy, frenulotomy, frenuloplasty (e.g. Z-plasty), tongue-tie division, and simple release; there may be variation in instrumentation, use of anesthetic, and extent of reconstruction

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2011. Health technology assessments, SRs

and meta-analyses were excluded if they were superseded by an update, or a more rigorous or recent review of the same studies. Primary clinical studies that were included within a SR of clinical evidence were excluded. Systematic reviews (SRs) with unique primary studies were excluded if the studies were limited to case series or case reports, in the interest of appraising higher quality evidence and acknowledgement of their limitations including small sample sizes, high risk of selection bias, and inability to determine causal relationships, comparative effectiveness, and disease frequency. Similarly SRs with unique primary studies that did not meet the inclusion criteria were excluded. Guidelines that were not developed using a systematic, evidence-based process were not included.

Critical Appraisal of Individual Studies

The included SRs were critically appraised using the AMSTAR checklist.[19] The methods used when conducting the literature search, study section, quality assessment, data extraction, and for pooling and summarizing the data were assessed. Primary clinical studies were critically appraised using Downs and Black.[20] Reporting, external validity, internal validity, and power were assessed. Summary scores were not calculated for the included studies; rather, a narrative description of the strengths and limitations of each included study is provided.

SUMMARY OF EVIDENCE

Quantity of Research Available

A total of 150 citations were identified in the literature search. Following screening of titles and abstracts, 126 citations were excluded and 24 potentially relevant reports from the electronic search were retrieved for full-text review. Two potentially relevant publications were retrieved from the grey literature search.

Excluded Studies

Of the 26 potentially relevant reports, 18 publications were excluded for various reasons. Five SRs were excluded because all included studies were included in a more recent or rigorous SR,[21,22] data was only available in abstract format[23,24] or because unique studies not included in other reviews were limited to case series or case reports.[25] One non-SR[26] was excluded on the basis of inadequate methodology. Four randomized controlled trials (RCTs)[27-30] and six non-randomized studies (NRSs)[31-37] were excluded as they were reviewed by an included SR. One abstract of a published RCT was excluded.[38] One NRS was excluded due to an inappropriate intervention.[36]

Included Studies

After exclusions, eight reports met the inclusion criteria and were reviewed. This included two SRs,[4,39,40] one published in two reports,[4,39] as well as one RCT[41] and four NRSs.[42-45] The PRISMA flowchart depicting study selection is presented in Appendix 1. Additional references of potential interest are provided in Appendix 6.

Summary of Study Characteristics

Two SRs (one presented in a full AHRQ report[4] as well as a journal article,[39] and one published in a single journal article[40]), one RCT,[41] and four NRSs[42-45] were identified regarding the clinical

effectiveness of frenectomy for the correction of ankyloglossia in newborns and infants. One SR reviewed three guidance documents, but no evidence-based guidelines were identified within the timeframe of the search. Detailed study characteristics are presented in Appendix 2.

Overlap between Systematic Reviews

There was substantial overlap in included studies between the SRs, which is summarized in Table A3. All of the included primary clinical studies in the review by Ito et al., were also included in the Agency for Healthcare Research and Quality (AHRQ) review, but they reported on additional clinical outcomes, as well as three unique guidance documents. Thus, the decision was made to review both SRs.

Study Design

Both SRs included RCTs, NRSs, and case series. One SR[4,39] also included case reports to inform harms data. One SR[4,39] reported all findings narratively, while the other[40] conducted meta-analysis for several outcomes. One SR included evidence from 58 unique publications in the main AHRQ report (six RCTs, 36 NRSs or case series, 15 case reports, 1 unpublished thesis).[4] Of these studies, the 29 publications (five RCTs and 24 NRSs or case series) regarding breastfeeding outcomes are presented in published journal article.[39] One SR[40] included evidence from 19 publications including four RCTs, 12 NRSs, two guidelines or guidance documents, and one position statement. The searches for the two SRs were current up to April 2013[40] and August 2014.[4,39]

Among the primary clinical studies identified, there was one RCT,[41] and four NRSs, including one cross-sectional survey,[42] two retrospective chart reviews,[44,45] and one prospective controlled before and after study.[43]

Country of Origin

The SRs were conducted by authors in the United States[4,39] and Japan.[40] One SR[4,39] reported on studies that were conducted in Australia, the United Kingdom, Korea, India, Israel, Brazil, Finland, Taiwan, Canada, the United States. The other SR[40] did not report on place of conduct, but given study overlap it can be assumed that the clinical studies were from the aforementioned countries. The guidance documents in this SR[40] presented were from the United Kingdom, the United States, and Canada. The RCT was conducted in Iran, and the NRSs in the United Kingdom,[42,45] the United States,[44] and Brazil.[43]

Patient Population

One SR[4,39] included children ages 0 to 18 years with ankyloglossia alone or concomitant lip-tie who were diagnosed by a clinical examiner using a variety of methods. The other SR[40] focused on neonates and infants less than six months of age with ankyloglossia and breastfeeding problems. The methods of diagnosing ankyloglossia used by the primary studies in this review were not reported.

The RCT[41] included children under 12 years old (mean = 32 months), and identified a subgroup of breastfeeding infants. Children had to be diagnosed with ankyloglossia based on Hazelbaker's appearance score ratings of greater than eight.

The NRSs included infants aged less than one week to less than eight weeks,[42] of unspecified age,[44] aged 30 days,[43] and with a median age of 38 days (range = 15 to 178 days).[45] All patients had to either have ankyloglossia or have undergone assessment for breastfeeding problems. Diagnoses were made using a midwife,[44] unspecified examiner,[44] or speech-language pathologist[43] to conduct a physical assessment. The method of diagnosis for one study was unclear.[45] None of the NRSs used a formal diagnostic tool to determine ankyloglossia rather relying on clinical assessment.

Interventions

One SR included studies investigating various methods of tongue-tie division including simple release (usually termed frenotomy, and sometimes frenectomy), laser release, and frenulectomy (e.g., Z-plasty).[4,39] One SR did not specify the specific surgical procedure of the included studies, indicating that the intervention was "frenotomy".[40] One SR[4,39] reported that the procedures were conducted by a range of health professionals including family, neonatal, and pediatric doctors, general, pediatric or specialty surgeons, and lactation or specialist consultants. The other SR[40] did not specify the qualifications of the health professionals conducting the procedure.

The procedures conducted in the RCT and NRSs included simple frenectomy,[41,43-45] and frenotomy plus advice on breastfeeding technique and positioning.[42] Breastfeeding advice or lactation support may have been provided in some of the other studies as part of the intervention, but it was not discussed.

Comparators

Both SRs[4,39,40] included primarily non-comparative studies; however, the comparative studies compared frenectomy to sham surgery, usual care (including but not limited to conventional lactation consultant support, supportive care, and bottle-feeding advice), and intensive lactation consultant support. Sham surgery involved taking the control patient into the procedure room for the same duration of time as the experimental group, without performing the procedure.

The RCT compared simple release to Z-plasty,[41] and two NRSs compared the procedure with no surgery[43] or support from an infant feeding consultant.[45] Two studies were non-comparative.[42,44]

Outcomes

The SRs reported on a range of outcomes including breastfeeding efficacy (both self-reported and observer ratings),[4,39,40] feeding outcomes,[4,39,40] functional outcomes (e.g., ability to clean teeth with tongue, lick lips etc.),[4,39] maternal breast or nipple pain,[4,39] milk supply,[40] weight gain,[40] adverse events,[4,39,40] and speech outcomes.[4,39] One SR[40] also presented information from three guidance reports on the use of frenectomy in patients with ankyloglossia.

The primary clinical studies reported on breastfeeding outcomes (both validated scales and self-reported accounts),[41-45] maternal nipple or breast pain,[41,42] speech outcomes,[41] functional outcomes,[41] parent satisfaction,[41] and feeding outcomes.[42]

Duration of Follow-Up

The majority of the evidence concerned relatively short-term outcomes. None of the high quality comparative studies looked at long-term outcomes.

For studies reviewed by the SRs, follow-up duration ranged from no follow-up (assessment completed immediately after procedure), to 2 weeks[40] or greater than 12 months.[4,39] Follow-up times were unclear for some primary studies included in the SRs.

Follow up for the primary clinical studies was three months,[41] various durations for a median of four months,[42] one month,[43,45] or none as the assessment was done immediately following the procedure.[44]

Summary of Critical Appraisal

Completed critical appraisal checklists are presented in Appendix 4.

Systematic Reviews

Design and Conduct of Search

A review protocol[46] was developed and posted by one SR.[4,39] The other made no reference to a protocol or a priori objectives so it is unclear whether all design elements and analyses were pre-planned.[40] One SR included duplicate study selection.[4,39] The number of authors involved in data extraction was unclear as one report indicated two reviewers[39] and one indicated that data was extracted by one reviewer and reviewed by another.[4] The other SR[40] did not disclose the number of reviewers involved in study selection and extraction. Lack of duplicate study selection increases the risk of overlooking potentially relevant literature, and lack of duplicate data extraction increases the risk of errors. Both SRs[4,39,40] conducted a comprehensive literature search using multiple databases. However, with the exception of searching of reference lists, no other grey literature search methods were disclosed. The searches were limited to English and Japanese language publications.[4,39,40] No date restrictions were noted with the exception of one database used in one SR,[40] which was searched from 1983 onward. Further, this SR failed to disclose search dates for two databases used. Neither SR[4,39,40] mentioned publication status as an exclusion criteria for the search, and one SR[4,39] included unpublished work.

Reporting

Both SRs provided information about included studies, though one SR[40] failed to present a list of included studies and presented study characteristics by clinical outcome. One SR[4,39] provided a list of excluded studies with reasons for exclusion. The other SR did not disclose a list of excluded studies.[40]

Quality Assessment

Both SRs[4,39,40] assessed study quality. One SR[4,39] used several tools and conducted quality appraisal in duplicate with input from content experts. The Cochrane Risk of Bias tool was used for RCTs, NRSs were assessed using tools based on the Research Triangle Institute item bank and McMaster Quality Assessment Scale of Harms. This quality assessment was used to inform a designation of strength of evidence as per AHRQ's Effective Health Care Program's Methods

Guide for Effectiveness and Comparative Effectiveness Reviews.[47] One SR[40] used Cochrane Risk of Bias and Grading of Recommendations, Assessment, Development and Evaluations (GRADE) criteria[48,49] to appraise the quality of studies and certainty of evidence and strength of recommendation. Both SRs discussed quality extensively in the presentation of results and conclusions. Overall, one SR[40] rated the evidence as high to moderate quality for breastfeeding efficacy, and weak for non-primary outcomes including milk supply, breastfeeding continuation, weight gain, and adverse events. The other SR reported mixed study quality, with RCTs generally being higher quality and NRSs and case series or reports typically being of lower quality, and the strength of evidence being low to insufficient for the majority of outcomes.[4,39]

Method of Pooling and Publication Bias

One SR[40] conducted meta-analyses for several outcomes; however, the appropriateness of this approach is debatable. The other SR[4,39] which reviewed all of the same primary clinical studies, concluded that "the small number of studies, the study designs and the heterogeneity of interventions and outcomes made a meta-analysis inappropriate" (page 43).[4] Consistent with this, the meta-analytic results of Ito et al.,[40] included a maximum of three studies per outcome, and all analyses reported high heterogeneity (I^2 = 81% to 90%). Also two pooled outcomes included NRSs of varying design. Thus, results from meta-analyses should be interpreted with caution. Publication bias was assessed informally by both SRs.[4,39,40] Publication bias was considered for each primary study as part of the evidence profile of one SR,[40] but the method used for assessment was unclear. One SR discussed publication bias in the limitations, noting that there was a possibility of publication bias, and that "most controlled studies reported only positive outcomes, and we identified no negative trials" (page 49).[4] Grey literature search methods were limited for both SRs[4,39,40] and no other methods of reducing publication bias (e.g., contacting authors and manufacturers, searching trial databases) were used, so publication bias in this literature base cannot be ruled out.

Conflict of Interest

Both SRs declared that there was no funding sources or affiliations that would result in conflict of interest.

Primary Clinical Studies

Reporting

All studies[41-45] described a hypothesis, aim, or objectives within their methods or introduction section, with the exception of the RCT[41] where it was only presented in the abstract. Two studies[43,45] described outcomes measures clearly. The RCT[41] did not explicitly list outcomes, and two studies only described outcomes in brief[42,44] until the results section. It was unclear whether study outcomes were pre-defined. All studies presented inclusion criteria with varying degrees of detail.[41-45] The RCT[41] described both the inclusion and exclusion criteria clearly. The NRSs[42-45] did not provide details about patient exclusion criteria. This is of concern as including patients with certain genetic disorders, concomitant malformations, and other clinical conditions, who were excluded from other reports, may affect the generalizability of the findings. In addition, two studies[42,43] provided very limited information about the inclusion criteria. The intervention of interest was clearly described by four of the studies.[41,43-45] One study[42] only gave the name of the intervention (i.e., frenotomy) and did not provide detail regarding the specific method of conduct. The distribution of potential confounders was underreported by all studies.[41-45] Studies

presented limited patient information, often in aggregate, rather than by group. Important confounders including method of diagnosis, degree of impairment or immobility, gender, ethnicity, maternal anatomy, milk supply, adjunct therapies, and relevant comorbidities were often unclear. As these factors have the potential to influence the relationship between frenectomy and breastfeeding or other clinical outcomes, the lack of information makes it difficult to assess their impact. Four studies[42-45] presented their main findings clearly; however, there was incomplete information about analytical approach in one case[42] and unclear statistical significance for some outcomes in another.[43] These issues made it difficult to interpret the results with certainty. The RCT[41] failed to present change from baseline statistics, despite making conclusions reflecting this comparison. In addition, there were some inconsistencies in the group means presented for between group differences and within group differences in some cases, but it is unclear whether this would have affected the observed outcomes.[41] Estimates of random variability were presented for the main outcomes for four studies.[41-43,45] One study reported simple rate estimates and did not provided any estimates of random variability.[44] Adverse events were generally underreported by all studies. The RCT[41] reported on intraoperative complications, bleeding, and adhesion, and one study[42] reported on major bleeding, infection and ulceration, but methods of assessing these outcomes was unclear. Adverse events were indicated as self-reported in one study and none were identified,[44] and two studies[43,45] did not comment on adverse events. Long term function issues, pain, and discomfort were not assessed by any study. Three studies[41,43,45] reported no dropouts or losses to follow-up. One[45] was a database study, so it is unclear whether there were eligible patients without follow-up data who weren't included in the study. One study conducted assessments immediately after surgery and no follow-up measures were made.[44] One study reported significant losses to follow-up due to missing questionnaire responses, and it is unclear how the patients who didn't respond differed from those who were included in analysis.[42] One study reported significant numbers of patients who refused the procedure.[43] It is unclear how these patients differed from the patients who received the surgery. The four studies that conducted statistical analysis all reported actual *P*-values.[41-43,45] One study didn't conduct any statistical tests.[44]

External Validity

None of the studies reported explicitly on sampling methods. In most cases the study sample was representative of the entire eligible population of children at the facility where the trial was being conducted. For example, the RCT included all eligible children attending pediatric surgery clinics over a two year period.[41] Two NRSs included all patients who attended an out-patient ankyloglossia clinic,[44] or all patients with documented tongue tie from a single hospital population.[45] All parents of children who had ankyloglossia and underwent frenectomy were contacted in one study.[42] Only patients whose parents agreed to frenectomy were included in another study, after screening by a speech language pathologist.[43] Regarding willing versus unwilling participants, two studies were retrospective chart reviews so all eligible patients were assessed.[44,45] Two studies mentioned that some patients either did not receive the procedure[43] or did not attend the clinic.[42] One study[42] reported that non-participants either sought alternative care or the reasons for not participating were unknown. Differences between willing and unwilling participants were unclear for two studies.[41,43] The settings and staff were generally highly specialized with a higher standard of care.[41-44] For instance, studies were conducted at pediatric surgery clinics at a teaching hospital,[41] a dedicated tongue-tie clinic,[42] specialized ankyloglossia clinic,[44] hospital with highly specialized assessment of patients.[43] One study did not provide details about the study setting.[45] Overall, the patients included in these studies appeared to be more visible (i.e., had chosen to attend a specialty clinic or undergo assessment

or procedure) and may have received a higher standard of care than all patients in the general ankyloglossia population who might be eligible for frenectomy.

Internal Validity – Bias

Patient blinding was not possible as the patient is awake during the procedure, but due to the patient age this is likely low risk. Similarly, the surgeons or health practitioners performing the surgery could not be blinded. None of the NRSs[42-45] blinded subjects, parents, or outcome assessors. The RCT[41] blinded parents, but it was unclear whether outcome assessors were blinded. No studies adjusted for different lengths of follow up. In four cases the duration of follow-up was reported to be the same between comparison groups.[41,43-45] One study[42] reported different lengths of follow-up with no adjustment. In this case it is unclear how this may have affected the outcomes observed. It is possible that shorter follow-up times may have been associated with better outcomes as they were closer to the intervention. The RCT[41] reported using paired t-tests for assessing differences between groups, which is appropriate for the change from baseline values, but not for between group comparisons as it increases the chance for false positives. Another study reported using analysis of variance tests to detect differences between groups, but there were only two comparison groups.[43] Again, this is not the appropriate statistical test, but in this case it is unlikely that it affected the outcome in a meaningful way.[43] One study did not describe the statistical tests used to assess the main outcomes, and did not use statistical tests to assess differences before and after the intervention at all time points. The statistical significance of differences presented for long-term follow-up is unclear.[42] One study did not conduct statistical analyses and only presented summary statistics.[44] One study used parametric statistics for continuous outcomes but due to the small sample sizes, non-parametric tests may have been more appropriate.[45] All studies had reliable compliance as it was a surgical intervention, but it is unclear whether there was compliance with other aspects of the treatment (e.g., following advice from lactation consultant, care of surgical site). The latter may have varied between and within study populations and may have to some extent contributed to variation in outcomes. For the majority of outcomes assessed by all primary studies, assessments were made by the mother and were subjective. In some cases nominal or ordinal scales were used but they appeared to be arbitrary.[41-44] These outcomes are subject to recall bias (e.g., when conducted retrospectively) and performance bias. Further, harms were self-reported in one study,[44] and appeared to be potentially self-reported in others.

Internal Validity – Confounding

Patients in all studies were recruited from the same populations including single hospitals,[41,42] an ankyloglossia clinic,[44] a hospital population screened for ankyloglossia,[43] and a group of patients diagnosed with tongue tie.[45] Patients in all studies were recruited over the same time period which ranged from five months to two years. The RCT[41] randomized patients using permuted block randomization with a block size of four. It is unclear whether random allocation was concealed. Regarding adjustment for confounders, all studies failed to present a comprehensive overview of baseline characteristics of study groups. In the case of the RCT[41] it was unclear whether there were significant baseline differences to account for. Two studies[42,44] stated that potential confounders were not assessed and could not be adjusted for. The remaining two studies,[43,45] did not adjust for any potential confounders, and did not describe reasons for this omission. Confidence in the results is limited due to lack of information regarding the potential risk of confounding, and lack of justification for not performing analyses (e.g., multivariate regression) to explore the influence of potential confounders on the effectiveness of frenectomy. Four studies reported either no follow-up time, were database

studies so there were no losses, or reported zero dropouts, and did not report planned methods of accounting for losses.[41,43-45] One study reported significant losses to follow-up and did not take them into account. As it is unclear how these patients differed from those who completed the study, the potential for bias is unclear.[42]

Power and Conflict of Interest

No power or sample size calculations were disclosed by any included study, so it is unclear whether there was sufficient power to detect the outcomes of interest. This is of particular concern where small sample[43,45] and imbalanced group[41,45] sizes were observed. None of the study authors noted any conflict of interest, financial or otherwise. Although one study did not explicitly disclose a conflict of interest statement.[45]

Summary of Findings

A detailed summary of study findings is provided in Appendix 5.

What is the clinical effectiveness of frenectomy for the correction of ankyloglossia in in newborns and infants?

Two SRs,[4,39,40] one RCT,[41] and four NRSs[42-45] addressed the clinical effectiveness of frenectomy for the correction of ankyloglossia in newborns and infants.

Breastfeeding Effectiveness

Regarding immediate or short-term maternally reported breastfeeding effectiveness, one SR[4,39] reported that maternally reported improvements in breastfeeding were observed by three studies, one that compared frenectomy to lactation consultant support at 48 hours,[50] one to sham surgery immediately after intervention,[27] and one to no intervention immediately post-procedure.[35] Based on the Breastfeeding Self-Efficacy Scale Short Form (BSES-SF) and HATLFF score, mothers reported significant improvements at five days in the group who received the procedure versus no intervention.[30] However, at 8 weeks the groups were similar, which may have been confounded by significant crossover of patients from the control to intervention group. One SR[40] pooled results from two RCTs and reported an increased likelihood of improved breastfeeding as evaluated by the mother in the group that received frenotomy compared to placebo. Of note, the incremental improvements were greater in the non-blinded[27] versus the blinded study.[50] Of the primary studies identified, one RCT reported that subjective breastfeeding scores improved following both simple release and Z-plasty procedures, with no differences observed between groups.[41] Further, jaw locking was improved following both procedures with no differences between groups, suggesting better latching.[41] One NRS[44] reported that the majority of mothers communicated that they experienced either a significant or moderate improvement in breastfeeding after correction of anterior or posterior ankyloglossia with or without concomitant lip-tie. The statistical significance of these findings is unclear as no analysis was conducted.[44] One NRS[43] reported a significant improvement in the average number of sucks in the three first groups of sucking after surgery in the infants who underwent frenotomy. Before surgery, quantity was lower than infants without tongue tie, and there were no differences after surgery. The same was observed for pause length.[43] One NRS[45] reported that maternal ratings of improvement in breastfeeding were higher in patients who received frenotomy, versus support from an infant feeding coordinator, and that this effect did

not differ in children older or younger than 30 days of age.[45] However, group sample sizes were small and imbalanced and results should be interpreted with caution.

Regarding long-term maternally reported outcomes, one SR[4,39] reported that based on longer-term follow-up data, the majority of mothers reported improved feeding, approximately half reported complete resolution of feeding issues, and the majority of infants were still breastfed at 3 and 4 to 5 months in one study.[51] No differences in breastfeeding effectiveness at 2 weeks,[28] or latch score at 8 weeks,[30] were reported by two other studies. One study[35] reported that a greater number of patients who received the procedure were still breastfeeding and for a longer duration than those who received no intervention. Similarly, a numerically lower proportion of patients reported discontinuation of breastfeeding due to pain.[35] None of the primary studies reported on long-term breastfeeding efficacy outcomes.

Regarding objective scales or measures of breastfeeding efficacy, one SR[4,39] reported on two studies that assessed the Infant Breastfeeding Assessment Tool (IBFAT) scores. One study reported significantly improved scores in the intervention group compared to sham surgery immediately after surgery but not at 2 weeks follow-up.[28] The other study reported no significant differences in IBFAT score at 5 days post-procedure.[30] One study assessed a score adapted from the LATCH tool (latch, audible swallowing, nipple type, mother's level of comfort, and help the mother needs to hold her infant to the breast) and IBFAT and reported 50% improvement in the intervention and 40% improvement in the control group, which was not significantly different.[27] One study assessed LATCH score alone and reported that there were no significant differences between the intervention and control group at 5 days post-intervention.[30] One SR[40] pooled results from two NRSs[52,53] and reported significant improvement in LATCH scores after frenotomy. This finding was supported by observational studies presented narratively in this review[40] which reported improvements in sucking or latch ranging from 57% to 92% after frenotomy.[22,54-57] Of the primary studies assessed, one NRS[45] reported significant improvements in IBFAT score in the frenotomy group post-intervention, while the scores in the control group stayed the same. Due to small and imbalanced group sample sizes these results may not be reliable.

Maternal Nipple Pain

One SR[40] conducted a meta-analysis of three NRSs[52,57,58] and reported that there was a significant reduction in nipple pain after the procedure. Two SRs[4,39,40] reported narratively on the findings of four RCTs.[27,28,30,55] Two studies reported no difference in pain scores versus sham operation immediately post-procedure[27] or after 5-days,[30] while the other two reported significant improvement in pain versus sham operation[28] and compared to pre-procedure values,[28,29] immediately,[28,29] and after four weeks.[28] One SR[40] presented further findings from five NRSs,[52,53,55,57,58] four of which suggested an improvement in pain scores following the procedure. Of the primary studies identified, one RCT[41] reported reduced breast pain in patients who received simple release or Z-plasty with no significant differences between groups. One NRS[42] reported a reduced incidence of breastfeeding related problems (e.g., breast pain and cracked nipples) at 48 hours and a mean follow-up of four months, although the long-term follow-up findings may be unreliable due to potential confounding and unclear statistical significance. One NRS reported that based on qualitative assessment of breastfeeding, the quantity of reported problems related to breastfeeding technique or effectiveness were reduced after the procedure.[43]

Feeding Sequelae and Growth

One SR[4,39] presented limited and primarily non-comparative evidence on feeding sequelae. Three studies suggested numerically greater improvements in feeding problems (i.e., dribbling and excess gas),[50] eating difficulty (i.e., ability to clean teeth with tongue, lick outside of lips and eat ice cream) at 3 years,[59] and a greater reduction in the number of breastfeeding and supplementary bottle feeding sessions at 2 weeks post-procedure.[55] One SR[40] reported on milk supply and production, noting a significant increase in milk transfer and 24 hour milk production in a sample of six mothers in one study.[52] Breastfeeding continuation rates were reported on by eight uncontrolled studies,[22,23,27,32,50,51,54,56] which suggested rates between 43% and 78% at 3 months, which was noted to be higher than the United Kingdom's national average of 29% by the authors.[40] A single study addressed weight gain and reported that neonates gained significant weight at 2 weeks post-procedure.[55] Of the primary studies identified, one NRS[42] reported an increase in the rate of exclusive breastfeeding at 48 hours, which trended back to baseline at a mean follow-up of four months. Formula milk use was reduced at 48 hours, but increased above baseline at follow-up.[42] No statistical analysis was conducted at long-term follow-up so the significance of these findings is unclear. This study[42] reported reduced odds of women reporting frequent or prolonged feed, shallow latch, and infant fussiness and restlessness at 48 hours.

Parent Satisfaction

Of the primary studies identified, one RCT[41] reported that Z-plasty resulted in greater parent satisfaction with the procedure versus simple release.

Harms

Adverse events of the procedure were mainly addressed by non-comparative evidence including case series and case reports, and were often self-reported. Both SRs[4,39,40] presented data on harms. The majority of studies reported no significant harms or minimal harms. The most common harm reported was minor and/or limited bleeding. Other potential harms were re-operation and scarring,[35] development of a healing slough requiring a week long recovery,[30] pain,[60] and case reports noted surgical site infection, swelling, post-surgical mucous cyst, and hemorrhagic shock after administration of procedure by an untrained worker.[61]

Of the primary studies identified, one RCT reported a single case of minor hemorrhage not requiring surgical intervention and a single case of re-operation.[41] One NRS[42] reported five cases of re-operation, in some case requiring multiple procedures. One NRS[44] reported no occurrences of self-reported complications

What are the evidence-based guidelines regarding frenectomy for the correction of ankyloglossia in newborns and infants?

No evidence-based guidelines were identified regarding frenectomy for the correction of ankyloglossia in newborns and infants. However, three older reports including one evidence-based guideline, one position statement, and one guidance statement were summarized in the SR by Ito et al.[40]

One evidence-based guideline,[62] one position statement,[2] and one guidance document,[63] provided suggestions regarding performing frenectomy. Although based on older evidence

and/or expert clinical opinion, they collectively suggested that when frenectomy is deemed appropriate, such as in the context of unresolved breastfeeding issues, it can be used to treat ankyloglossia and administered by a qualified healthcare provider with no major safety concerns.

Limitations

Validity of Outcome Measures

The majority of observations regarding the main outcome of interest, breastfeeding efficacy, as well as other outcomes like maternal breast and nipple pain were subjective in nature. Maternal perspectives and ratings may be subject to performance bias. For the comparative studies, it was very difficult to blind parents, as sham surgery could easily be unblinded by observing the child's oral anatomy. Even standardized scales used to improve consistency in the assessment breastfeeding outcomes may be vulnerable to subjectivity by the outcome assessor, particularly due to difficulty blinding and the reliance on visual assessment as well as the presence of maternally reported outcomes embedded in many of these tools. Further, many outcomes were only assessed in the short-term, either immediately after surgery or shortly afterwards. Results do not address longer-term outcomes such as extended breastfeeding success and growth outcomes in the child.

Variation in Diagnostic Approach

The approach that is taken to identify ankyloglossia may vary based on several factors including expertise and tools available to the assessor, setting (e.g., specialized clinic versus primary care), and severity of the condition. Level of expertise in particular might introduce issues when the assessor is unfamiliar with nuanced elements of ankyloglossia assessment such as visualizing posterior ankyloglossia and concomitant upper-lip tie, which are difficult to do.[44,64] Hazelbaker's criteria, and specific physical criteria of varying complexity are the most common approaches used.[7] Variation in diagnostic procedure is problematic as it introduces inconsistency in patient selection, and none of these methods have been validated. Also, standardized approaches have their drawbacks as they may be lengthy and cumbersome to apply. It has been observed that delaying the procedure in the interest of conducting a thorough assessment may increase the age at the time of the procedure, which may be detrimental to the child, as well as the number of mothers unable to breastfeed.[36] Further research is needed to establish standards for the diagnosis of ankyloglossia that emphasize efficiency and standardization. As was observed across the clinical studies evaluated in this report, many different approaches have been taken to identify patients. These inconsistencies may limit the generalizability of individual study findings as it is unclear whether patients with more or less severe conditions, or with various comorbidities or alternative causes of breastfeeding problems were included in the study populations. Further, it was often unclear whether breastfeeding problems were a criteria for receiving the procedure. Where breastfeeding issues were not present, there may have been a lower likelihood of observing a benefit.

Reliability and Generalizability of Safety Data

While there is a perception that this is a low risk procedure, the majority of the safety evidence comes from small studies that often rely on self-reporting to inform adverse events. This could contribute to underreporting of harms, particularly minor harms that don't require medical intervention, but that may still be relevant to the parents of a child trying to decide whether to

proceed with a frenectomy. Further, potential harms may depend on who is conducting the procedure, the surgical method, and the age of the patient. For instance, there may be a lower risk of harms if the procedure is conducted by a highly trained physician versus a minimally trained community health worker. Serious harms were observed in a single case series reviewed within this report as a result of the procedure being conducted by untrained personnel.

Potential Heterogeneity in Clinical Status of Patients

While some studies described patient populations in detail, others did not distinguish between posterior and anterior ankyloglossia, patients with concomitant lip-tie or other comorbid conditions, or severity of the condition. Accordingly, results may not be generalizable to patients with different combinations or severity of these disorders. Due to the exclusion of patients with comorbidities and other conditions related to craniofacial malformation or genetic conditions that might otherwise explain ankyloglossia or breastfeeding problems, results may only apply to patients who are otherwise healthy rather than more complex clinical populations. As was observed by a single NRS reviewed within this report, outcomes may be different depending on the classification of the patient. Thus, interpretation of evidence whether specific patient characteristics are unclear is difficult, and results from studies in very specific patients may not be generalizable to the wider population.

Terminology Issues and Variation in Intervention

As indicated in the inclusion criteria of this report, there are many different synonyms for frenectomy, which may in some case indicate the same procedure, and in others may indicate different instrumentation (e.g., laser versus scalpel), or a different degree of complexity (e.g., simple release versus Z-plasty). It has been proposed that some methods may be more effective, or at least more tolerable for the patient than others. Also, studies may have used different adjunct therapies such as anesthetic, analgesics, or post-surgical support such as lactation consultants. This suggests limited comparability across studies that provided different treatments, and suggest that pooling studies or making common observations about different procedures should be approached with caution. Also, there were several cases where studies failed to distinguish the exact approach to tongue-tie splitting that was used, making it difficult to interpret how the findings may be applied.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

The use of frenectomy to treat ankyloglossia in neonates and infants with breastfeeding problems appears to be safe and may confer benefit to the mother and baby. However, the results should be interpreted with consideration of the subjectivity of outcome measures; generalizability issues due to differences in patient populations, procedure, and outcome measures; lack of information on long-term benefits and harms; unclear influence of potential confounders; and questionable reliability of pooled and poor quality findings.

The reviewed evidence collectively suggests that tongue-tie division likely has a positive impact on maternally reported or perceived breastfeeding effectiveness in the short-term. Benefit is less clear for long-term outcomes, and objective measurements of breastfeeding effectiveness such as the IBFAT or LATCH tools. Evidence regarding breast and nipple pain is also mixed; however, more studies reported improvements in pain following the procedure, and some variability may be attributable to differences pain measurement tools. There is also limited evidence to indicate that frenectomy may improve feeding problems including infant symptoms

and milk supply, allowing for longer continuation of breastfeeding and proper weight gain, but the strength of these observations tended to wane over time. The procedure was demonstrated to be safe and tolerable, with many studies reporting no adverse events. The most frequent complaints included minor bleeding, scarring and requirement for further procedures or re-operation. Older guidance is consistent with the clinical evidence, stating that in appropriate circumstances (e.g., ankyloglossia with associated breastfeeding problems), frenectomy is safe, may result in benefits, and should be conducted by a trained health professional.

The evidence underlying these conclusions comes primarily from poor-quality NRSs, and does not adequately address the question of whether frenectomy provides a meaningful incremental benefit over other treatments or procedures to improve breastfeeding, particularly in the long-term. Many potential confounders that could have contributed to variation in the observed outcomes were not controlled for. Factors such as the mother's anatomy, milk supply, comorbid causes of feeding problems, specific surgical method, qualifications of staff performing the surgery, and adherence to post-surgical advice and adjunct breastfeeding suggestions should be measured and considered in future studies if possible. Future research is needed to standardize diagnostic procedures, develop evidence-based eligibility criteria, and to assess the impact of multiple confounders on the effectiveness of the procedure. As evidenced by variation in benefit and harms observed across studies, the success of the procedure may depend on the context. As such, results may not be generalizable to older patients, patients receiving care in community or outpatient settings or by untrained professionals, and patients with more severe disability. Based on the evaluated strength of current evidence, results from future and ongoing studies (see Appendix 6) have the potential to influence the observed effectiveness of the procedure. Results from these trials may resolve some of the remaining uncertainty.

Altogether, given the minimal harms and probable benefit, albeit of uncertain magnitude, frenectomy may be a viable treatment option for infants of mothers who wish to breastfeed and are experiencing difficulty.

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REFERENCES

1. Breastfeeding [Internet]. Geneva: World Health Organization; 2016. [cited 2016 Jun 2]. Available from: http://www.who.int/topics/breastfeeding/en/

2. Nutrition for healthy term infants: recommendations from birth to six months. A joint statement of Health Canada, Canadian Paediatric Society, Dietitians of Canada, and Breastfeeding Committee for Canada [Internet]. Ottawa: Health Canada; 2015 Aug 18. [cited 2016 Jun 2]. Available from: http://www.hc-sc.gc.ca/fn-an/nutrition/infant-nourisson/recom/index-eng.php

3. Gionet L. Health at a glance. Breastfeeding trends in Canada [Internet]. Ottawa: Statistics Canada; 2015 Nov 27. [cited 2016 Jun 2]. (Catalogue no. 82-624-X). Available from: http://www.statcan.gc.ca/pub/82-624-x/2013001/article/11879-eng.htm

4. Francis DO, Chinnadurai S, Morad A, Epstein RA, Kohanim S, Krishnaswami S, et al. Treatments for ankyloglossia and ankyloglossia with concomitant lip-tie [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2015 May. [cited 2016 May 18]. (AHRQ Comparative Effectiveness Reviews). Available from: www.effectivehealthcare.ahrq.gov/reports/final.cfm

5. Han SH, Kim MC, Choi YS, Lim JS, Han KT. A study on the genetic inheritance of ankyloglossia based on pedigree analysis. Arch Plast Surg [Internet]. 2012 Jul [cited 2016 Jun 7];39(4):329-32. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3408277

6. Hong P. Five things to know about...ankyloglossia (tongue-tie). CMAJ [Internet]. 2013 Feb 5 [cited 2016 Jun 2];185(2):E128. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3563913

7. Segal LM, Stephenson R, Dawes M, Feldman P. Prevalence, diagnosis, and treatment of ankyloglossia: methodologic review. Can Fam Physician [Internet]. 2007 Jun [cited 2016 Jun 2];53(6):1027-33. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1949218

8. Ngerncham S, Laohapensang M, Wongvisutdhi T, Ritjaroen Y, Painpichan N, Hakularb P, et al. Lingual frenulum and effect on breastfeeding in Thai newborn infants. Paediatr Int Child Health. 2013 May;33(2):86-90.

9. Ingram J, Johnson D, Copeland M, Churchill C, Taylor H, Emond A. The development of a tongue assessment tool to assist with tongue-tie identification. Arch Dis Child Fetal Neonatal Ed [Internet]. 2015 Jul [cited 2016 May 20];F1-F5. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4484383

10. Division of ankyloglossia (tongue-tie) for breastfeeding [Internet]. London: National Institute for Health and Care Excellence (NICE); 2005 Dec 14. [cited 2016 May 20]. (Interventional procedure guidance; no. 149). Available from: https://www.nice.org.uk/guidance/ipg149/resources/division-of-ankyloglossia-tonguetie-for-breastfeeding-1899863228061637

11. Messner AH, Lalakea ML, Aby J, Macmahon J, Bair E. Ankyloglossia: incidence and associated feeding difficulties. Arch Otolaryngol Head Neck Surg. 2000 Jan;126(1):36-9.

12. Messner AH, Lalakea ML. The effect of ankyloglossia on speech in children. Otolaryngol Head Neck Surg. 2002 Dec;127(6):539-45.

13. Ricke LA, Baker NJ, Madlon-Kay DJ, DeFor TA. Newborn tongue-tie: prevalence and effect on breast-feeding. J Am Board Fam Pract [Internet]. 2005 Jan [cited 2016 Jun 2];18(1):1-7. Available from: http://www.jabfm.org/content/18/1/1.full.pdf+html

14. Kara C. Evaluation of patient perceptions of frenectomy: a comparison of Nd:YAG laser and conventional techniques. Photomed Laser Surg. 2008 Apr;26(2):147-52.

15. Joseph KS, Kinniburgh B, Metcalfe A, Razaz N, Sabr Y, Lisonkova S. Temporal trends in ankyloglossia and frenotomy in British Columbia, Canada, 2004-2013: a population-based study. CMAJ Open [Internet]. 2016 Jan 26 [cited 2016 Jun 2];4(1):E33-E40. Available from: http://cmajopen.ca/content/4/1/E33.full.pdf+html

16. Messner AH, Lalakea ML. Ankyloglossia: controversies in management. Int J Pediatr Otorhinolaryngol. 2000 Aug 31;54(2-3):123-31.

17. Lalakea ML, Messner AH. Ankyloglossia: does it matter? Pediatr Clin North Am. 2003 Apr;50(2):381-97.

18. Rowan-Legg A. Ankyloglossia and breastfeeding [Internet]. Ottawa: Canadian Paediatric Society; 2015 May 11. [cited 2016 May 20]. (Position statement). Available from: http://www.cps.ca/documents/position/ankyloglossia-breastfeeding

19. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol [Internet]. 2007 [cited 2016 Jun 14];7:10. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1810543/pdf/1471-2288-7-10.pdf

20. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health [Internet]. 1998 Jun [cited 2016 Jun 14];52(6):377-84. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1756728/pdf/v052p00377.pdf

21. Burrows S, Lanlehin R. Is frenotomy effective in improving breastfeeding in newborn babies with tongue-tie? A literature review. British Journal of Midwifery. 2015;23(11):8p.

22. Finigan V, Long T. The effectiveness of frenulotomy on infant-feeding outcomes: a systematic literature review [Internet]. London: Royal College of Midwives; 2013 May. [cited 2016 May 20]. Available from: https://www.rcm.org.uk/learning-and-career/learning-and-research/ebm-articles/the-effectiveness-of-frenulotomy-on-infant

23. O'Shea JE, Foster JP, Jacobs SE, O'Donnell CPF, Davis PG. Frenotomy for tongue-tie in newborn infants. J Paediatr Child Health [Internet]. 2014 [cited 2016 May 18];50(Suppl 1):25. Available from: http://onlinelibrary.wiley.com/doi/10.1111/jpc.12528/epdf

24. Constantine AH, Williams C, Sutcliffe AG. A systematic review of frenotomy for ankyloglossia (tongue tie) in breast fed infants. Arch Dis Child. 2011;96:A62-A63.

25. Webb AN, Hao W, Hong P. The effect of tongue-tie division on breastfeeding and speech articulation: a systematic review. International Journal of Pediatric Otorhinolaryngology. 2013;77(5):635-46.

26. Kumar M, Kalke E. Tongue-tie, breastfeeding difficulties and the role of frenotomy. Acta Paediatr. 2012 Jul;101(7):687-9.

27. Berry J, Griffiths M, Westcott C. A double-blind, randomized, controlled trial of tongue-tie division and its immediate effect on breastfeeding. Breastfeeding medicine : the official journal of the Academy of Breastfeeding Medicine. 2012;7(3):189-93.

28. Buryk M, Bloom D, Shope T. Efficacy of neonatal release of ankyloglossia: a randomized trial. Pediatrics [Internet]. 2011 Aug [cited 2016 May 18];128(2):280-8. Available from: http://pediatrics.aappublications.org/content/pediatrics/128/2/280.full.pdf

29. Dollberg S, Botzer E, Grunis E, Mimouni FB. Immediate nipple pain relief after frenotomy in breast-fed infants with ankyloglossia: a randomized, prospective study. J Pediatr Surg. 2006 Sep;41(9):1598-600.

30. Emond A, Ingram J, Johnson D, Blair P, Whitelaw A, Copeland M, et al. Randomised controlled trial of early frenotomy in breastfed infants with mild-moderate tongue-tie. Arch Dis Child Fetal Neonatal Ed [Internet]. 2014 May [cited 2016 May 18];99(3):F189-F195. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3995264

31. Dollberg S, Marom R, Botzer E. Lingual frenotomy for breastfeeding difficulties: a prospective follow-up study. Breastfeed Med. 2014 Jul;9(6):286-9.

32. Mettias B, O'Brien R, bo Khatwa MM, Nasrallah L, Doddi M. Division of tongue tie as an outpatient procedure. Technique, efficacy and safety. Int J Pediatr Otorhinolaryngol. 2013 Apr;77(4):550-2.

33. O'Callahan C, Macary S, Clemente S. The effects of office-based frenotomy for anterior and posterior ankyloglossia on breastfeeding. Int J Pediatr Otorhinolaryngol. 2013 May;77(5):827-32.

34. Sethi N, Smith D, Kortequee S, Ward VM, Clarke S. Benefits of frenulotomy in infants with ankyloglossia. Int J Pediatr Otorhinolaryngol. 2013 May;77(5):762-5.

35. Steehler MW, Steehler MK, Harley EH. A retrospective review of frenotomy in neonates and infants with feeding difficulties. Int J Pediatr Otorhinolaryngol. 2012 Sep;76(9):1236-40.

36. Todd DA, Hogan MJ. Tongue-tie in the newborn: early diagnosis and division prevents poor breastfeeding outcomes. Breastfeed Rev. 2015 Mar;23(1):11-6.

37. Toner D, Giordano T, Handler SD. Office frenotomy for neonates: resolving dysphagia, parental satisfaction and cost-effectiveness. ORL Head Neck Nurs. 2014;32(2):6-7.

38. Sutcliffe AG, Whitelaw A, Ingram J, Emond A. A feasability randomised controlled single blind parallel group trial for frenotomy in tongue tied breast fed babies with mild to moderate tongue tie. Arch Dis Child. 2014;99:A162.

39. Francis DO, Krishnaswami S, McPheeters M. Treatment of ankyloglossia and breastfeeding outcomes: a systematic review. Pediatrics [Internet]. 2015 Jun [cited 2016 May 18];135(6):e1458-e1466. Available from: http://pediatrics.aappublications.org/content/pediatrics/135/6/e1458.full.pdf

40. Ito Y. Does frenotomy improve breast-feeding difficulties in infants with ankyloglossia? Pediatr Int. 2014 Aug;56(4):497-505.

41. Yousefi J, Tabrizian Namini F, Raisolsadat SM, Gillies R, Ashkezari A, Meara JG. Tongue-tie Repair: Z-plasty vs simple release. Iran J Otorhinolaryngol [Internet]. 2015 Mar [cited 2016 May 18];27(79):127-35. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4409957

42. Braccio S, Chadderton Z, Sherridan A, Upadhyaya M. Tongue-tie division. Is it worth it? A retrospective cohort study. British Journal of Midwifery. 2016 May;24(5):5p.

43. Martinelli RL, Marchesan IQ, Gusmao RJ, Honorio HM, Berretin-Felix G. The effects of frenotomy on breastfeeding. J Appl Oral Sci [Internet]. 2015 Mar [cited 2016 May 18];23(2):153-7. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4428459

44. Pransky SM, Lago D, Hong P. Breastfeeding difficulties and oral cavity anomalies: The influence of posterior ankyloglossia and upper-lip ties. Int J Pediatr Otorhinolaryngol. 2015 Oct;79(10):1714-7.

45. Sharma SD, Jayaraj S. Tongue-tie division to treat breastfeeding difficulties: our experience. J Laryngol Otol. 2015 Oct;129(10):986-9.

46. Ankyloglossia [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2014 Jun 30. [cited 2016 Jun 7]. (Evidence-based practice centre systematic review protocol). Available from: https://effectivehealthcare.ahrq.gov/ehc/products/558/1931/Ankyloglossia-protocol-140630.pdf

47. Methods guide for effectiveness and comparative effectiveness reviews [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2014 Jan. Report No.: 10(14)-EHC063-EF. [cited 2016 Jun 7]. Available from: https://effectivehealthcare.ahrq.gov/ehc/products/60/318/CER-Methods-Guide-140109.pdf

48. Schunemann HJ, Brozek J, Guyatt GH, Oxman AD, eds. GRADE handbook. Hamilton (ON): GRADE working group; 2013 Oct.

49. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ [Internet]. 2008 Apr 26 [cited 2016 Jun 7];336:924-6. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2335261/pdf/bmj-336-7650-analysis-00924.pdf

50. Hogan M, Westcott C, Griffiths M. Randomized, controlled trial of division of tongue-tie in infants with feeding problems. J Paediatr Child Health. 2005 May;41(5-6):246-50.

51. Khoo AK, Dabbas N, Sudhakaran N, de-Ajayi N, Patel S. Nipple pain at presentation predicts success of tongue-tie division for breastfeeding problems. Eur J Pediatr Surg. 2009 Dec;19(6):370-3.

52. Geddes DT, Langton DB, Gollow I, Jacobs LA, Hartmann PE, Simmer K. Frenulotomy for breastfeeding infants with ankyloglossia: effect on milk removal and sucking mechanism as imaged by ultrasound. Pediatrics. 2008 Jul;122(1):e188-e194.

53. Srinivasan A, Dobrich C, Mitnick H, Feldman P. Ankyloglossia in breastfeeding infants: the effect of frenotomy on maternal nipple pain and latch. Breastfeed Med. 2006;1(4):216-24.

54. Masaitis NS, Kaempf JW. Developing a frenotomy policy at one medical center: a case study approach. J Hum Lact. 1996 Sep;12(3):229-32.

55. Miranda BH, Milroy CJ. A quick snip - A study of the impact of outpatient tongue tie release on neonatal growth and breastfeeding. J Plast Reconstr Aesthet Surg. 2010 Sep;63(9):e683-e685.

56. Griffiths DM. Do tongue ties affect breastfeeding? J Hum Lact. 2004 Nov;20(4):409-14.

57. Argiris K, Vasani S, Wong G, Stimpson P, Gunning E, Caulfield H. Audit of tongue-tie division in neonates with breastfeeding difficulties: how we do it. Clin Otolaryngol. 2011 Jun;36(3):256-60.

58. Ballard JL, Auer CE, Khoury JC. Ankyloglossia: assessment, incidence, and effect of frenuloplasty on the breastfeeding dyad. Pediatrics [Internet]. 2002 [cited 2016 Jun 7];110(5). Available from: http://pediatrics.aappublications.org/content/110/5/e63

59. Walls A, Pierce M, Wang H, Steehler A, Steehler M, Harley EH, Jr. Parental perception of speech and tongue mobility in three-year olds after neonatal frenotomy. Int J Pediatr Otorhinolaryngol. 2014 Jan;78(1):128-31.

60. Puthussery FJ, Shekar K, Gulati A, Downie IP. Use of carbon dioxide laser in lingual frenectomy. Br J Oral Maxillofac Surg. 2011 Oct;49(7):580-1.

61. Opara PI, Gabriel-Job N, Opara KO. Neonates presenting with severe complications of frenotomy: a case series. J Med Case Rep [Internet]. 2012 [cited 2016 Jun 7];6:77. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3310719

62. Division of ankyloglossia (tongue-tie) for breastfeeding: understanding NICE guidance - information for people considering the procedure for their baby, and for the public [Internet]. London: National Institute for Health and Care Excellence (NICE); 2005 Dec. 12 p. [cited 2016 May 20]. (Information about NICE interventional procedure guidance; no. 149). Available from: https://www.nice.org.uk/guidance/ipg149/resources/division-of-ankyloglossia-tongue-tie-for-breastfeeding-304342237

63. The Academy of Breastfeeding Medicine Protocol Committee, Ballard J. Protocol # 11: Guidelines for the evaluation and management of neonatal ankyloglossia and its complications in the breastfeeding dyad. In: ABM protocols [Internet]. New Rochelle (NY): Academy of Breastfeeding Medicine; 2004 [cited 2016 May 20]. Available from: http://www.bfmed.org/Media/Files/Protocols/ankyloglossia.pdf

64. Kupietzky A, Botzer E. Ankyloglossia in the infant and young child: clinical suggestions for diagnosis and management. Pediatric Dentistry [Internet]. 2005 [cited 2016 Jun 7];27:40-6. Available from: http://www.aapd.org/assets/1/25/kupietzky-27-1.pdf

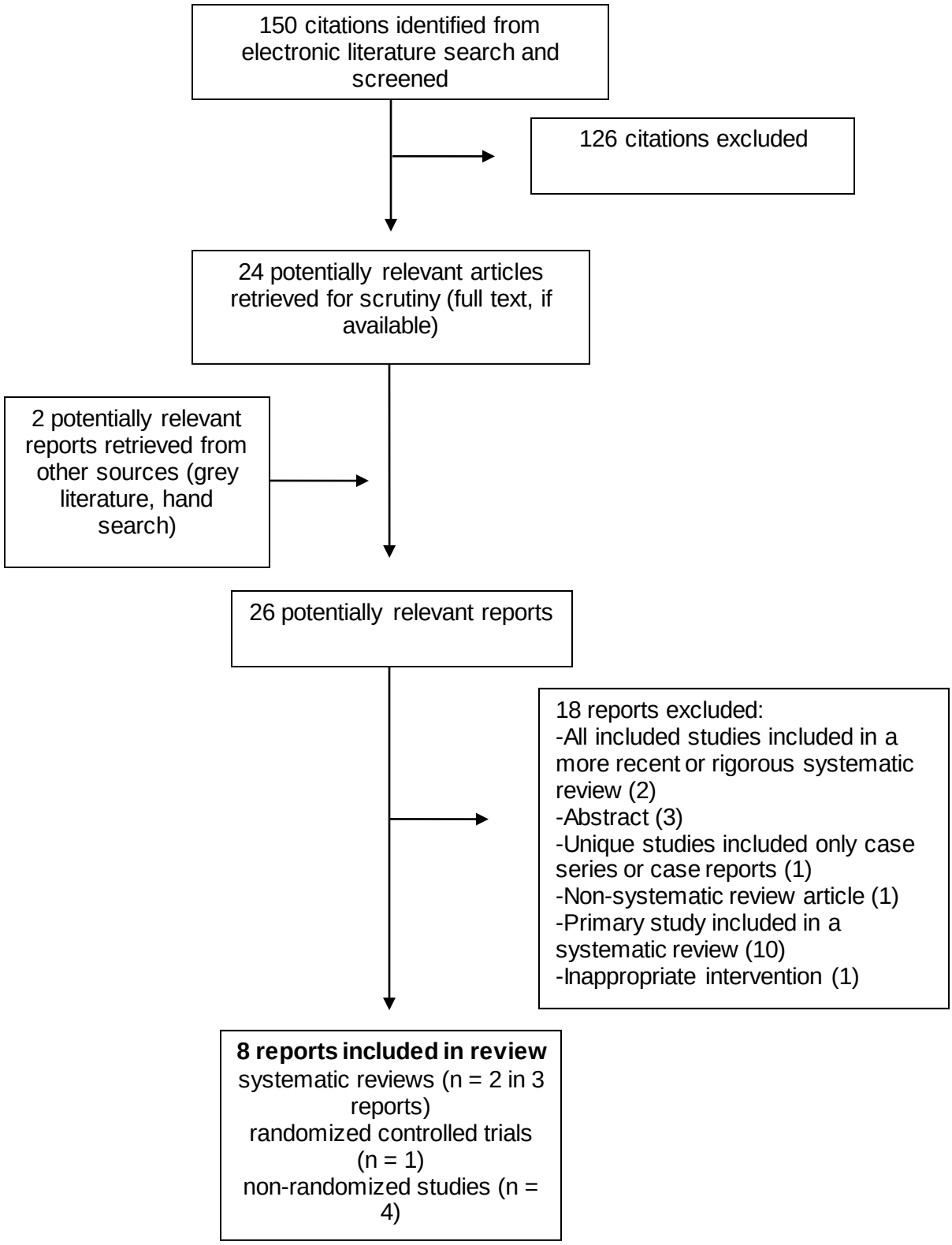
65. Dave J, Sinha V, Barot D, Modi N, Gurnani D, Patel T. Speech disorders encountered in routine ENT practice and the role of speech therapy in its effective management. Indian Journal of Otology [Internet]. 2013 Oct [cited 2016 Jun 10];19(4):169-72. Available from: http://www.indianjotol.org/article.asp?issn=0971-7749;year=2013;volume=19;issue=4;spage=169;epage=172;aulast=Dave

66. Godley FA. Frenuloplasty with a buccal mucosal graft. Laryngoscope. 1994 Mar;104(3 Pt 1):378-81.

67. Amir LH, James JP, Beatty J. Review of tongue-tie release at a tertiary maternity hospital. J Paediatr Child Health. 2005 May;41(5-6):243-5.

68. Ridgers I, McCombe K, McCombe A. A tongue-tie clinic and service. British Journal of Midwifery. 2013 Sep;17(4).

Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table A1: Characteristics of Included Systematic Reviews and Meta-Analyses

First Author, Publication Year, Country; Databases and Search Dates	Types and Numbers of Studies	Population Characteristics, Method of Diagnosis	Intervention	Comparator(s)	Clinical Outcomes, Length of Follow-Up
Francis, 2015, United States[39] and Francis, 2015 (AHRQ)[4] Medline, CINAHL, EMBASE, PsychINFO (no date restrictions, inception to August 2014)	n = 29 studies (5 RCTs, 1 retrospective cohort, 23 case series) presented in journal article regarding breastfeeding outcomes;[39] 58 unique publications reviewed in the full report;[4 a] Studies conducted in the United States, Canada, Europe, Asia or Other	Children ages 0 to 18 with ankyloglossia or ankyloglossia with concomitant tight labial frenulum (lip-tie), total n = 5785;[b] Diagnosed by clinician examination using various methods including HATLFF or LATCH scores, or unspecified diagnostic criteria	Surgical interventions (simple anterior frenectomy, laser frenulectomy, posterior frenulectomy, Z-plasty repair);[c] Performed by family practitioners, pediatricians, otolaryngologists, otolaryngologist consultant, lactation consultant, pediatric surgeon, neonatologist, pediatric dentist, general surgeon, or not reported	Sham surgery, [d] usual care, intensive lactation consultation	Breastfeeding efficacy (maternally reported or observer ratings)[4,39] Nipple pain (maternally reported)[4,39]; Follow-up: Ranged from no follow-up to > 12 months; unclear in 8 reports
Ito, 2014[40] PubMed, Japana Centra Revuo Medicina, CINAHL, Cochrane Library (inception to April 2013)	n = 19 reports (n = 4 RCTs, n = 12 non-randomized studies, n = 2 guidelines, n = 1 position statement)	Neonates and infants (<6 months of age) with poor breastfeeding and ankyloglossia, total sample size unclear (n = 97 to 123 in meta-analysis)[e] Method of diagnosis of ankyloglossia not reported	Frenotomy Qualifications of health professional conducting procedure not reported	Lactation support alone, sham surgery, usual care	Breastfeeding effectiveness, feeding outcomes, adverse events Follow-up: Ranged from no follow-up to 2 weeks or not reported

HATLFF = Hazelbaker Assessment Tool of Lingual Frenulum Function; LATCH = Latch, Audible swallowing, Type of nipple, Comfort, Hold

[a] Effectiveness data only extracted from comparative studies; harms data from comparative and non-comparative studies; while most non-randomized studies were identified as case-series not all were descriptive and non-comparative

[b] Patients with Van der Woude syndrome, Pierre Robin syndrome, Down syndrome, or craniofacial abnormalities, as well as premature infants)< 27 weeks of gestation) were excluded

[c] Also addressed non-surgical interventions such as complementary and alternative medicine therapies, lactation intervention, speech therapy, physical therapy, oral motor therapy, and stretching exercises/therapy

[d] Taking infant to intervention room for the same duration as infants receiving the procedure

[e] Excluding patients suffering from other oral anomalies and central nervous system disturbances

Table A2: Characteristics of Included Clinical Studies

First Author, Publication Year, Country	Study Design	Patient Characteristics	Method of Diagnosis or Assessment of Ankyloglossia	Intervention(s)	Comparator(s)	Clinical Outcomes, Follow-Up
Randomized Controlled Trials						
Yousefi, 2015, Iran[41]	RCT[a] (permuted blocks with block size of 4)	Children (n = 27 to n = 50 depending on outcome) under the age of 12 (range 5 days to 8 years, mean = 32 months)[b]	Hazelbaker's appearance score > 8, Initiated by the mother or physician	Frenulotomy (simple release without suturing) n = 9 of breastfeeding age (77% of mothers reported milking pain	Frenuloplasty (Z-plasty with opposing 60° triangular flaps alternated and sutured) n = 18 of breast-feeding age 44% of mothers reported milking pain	Within group (non-comparative) and between group differences presented for: • Breastfeeding frequency • Mastalgia (Breast Pain) • Word articulation • Tongue movement • Jaw locking • Tongue elongation • Parental satisfaction; Follow-up = 3 months
Non-Randomized Studies						
Braccio, 2016, United Kingdom[42]	Cross-sectional survey (retrospective data)	Parents of patients who attended a tongue-tie-clinic at London Children's Hospital from October 2013 to September 2014; Children were aged <1 week to >8 weeks (10 cases age was unclear) range was 1 day to 5 months (Infants with breastfeeding difficulties and suspected tongue tie [n = 158])	No formal tool used to diagnose ankyloglossia Referred by postnatal ward midwives, community midwives, breastfeeding consultants, GPs, health visitors, general paediatrics consultants, paediatric surgery consultants, and neonatal consultants;	Frenotomy plus advice on breastfeeding technique and positioning	No comparator	Before procedure, first 48 hours after, and at time of follow-up all collected retrospectively Breastfeeding problems (maternal problems like breast pain, issues affecting the feed (frequent or long feeds, shallow latch, fussiness or restlessness of the

Table A2: Characteristics of Included Clinical Studies

First Author, Publication Year, Country	Study Design	Patient Characteristics	Method of Diagnosis or Assessment of Ankyloglossia	Intervention(s)	Comparator(s)	Clinical Outcomes, Follow-Up
			Experienced midwife assessed breastfeeding to determine that restriction in infants tongue movement was present and those with confirmed diagnosis (unclear method) underwent frenotomy			infant);[c] Follow-up: Infants between 2 weeks and 9 months of age at follow-up, median follow-up 4 months
Pransky, 2015, United States[44]	Retrospective chart review (January 2014 to December 2014)	Infants of unspecified age (n = 618) with anterior or posterior ankyloglossia, upper-lip tie or a combination of conditions (otherwise healthy) who attended a biweekly half-day outpatient ankyloglossia clinic run by a otolaryngology-physician assistant rained in assessing and managing various oral cavity anomalies and supervised by the pediatric otolaryngologist, over a period of one year (January to December 2014) 290 (47%) with anterior ankyloglossia; 120 (19%) with posterior ankyloglossia, and 14 (2%) had upper-lip tie; 33 (5%) had posterior ankyloglossia and upper-lip tie	Full head and neck examination (palpation of floor of mouth and lingual frenulum) Grading of ankyloglossia (posterior or anterior type I to IV) subjectively determined by examiner based on physical prominence, tightness, an location of the lingual frenulum on inspection and palpation as well as on the apparent limitation of tongue movement and notching of the tongue lip	Simple tongue-tie release (grooved director used to isolate lingual frenulum, straight hemostat clamp placed on frenulum, clamp removed after a few seconds and lingual frenulum incised using an iris scissor. Release maneuver performed far posteriorly to open up the mucosal reflection to ensure changes of recurrence low; Patients instructed to perform stretching and massaging exercises under the tongue before each feeding for five days to reduce scar band formation, and encouraged to see lactation consultants or breastfeeding specialists	No comparator	Breastfeeding improvement after release procedure; Follow-up – none, measurement taken immediately after procedure

Table A2: Characteristics of Included Clinical Studies

First Author, Publication Year, Country	Study Design	Patient Characteristics	Method of Diagnosis or Assessment of Ankyloglossia	Intervention(s)	Comparator(s)	Clinical Outcomes, Follow-Up
Martinelli, 2015, Brazil[43]	Controlled before-and-after study	30 day old infants with tongue-tie (n = 28) [d]	Assessed by a speech-language pathologist	Frenotomy	No surgery	Breastfeeding assessment at 30 days and 75 days old; Follow-up = 75 days (30 days post surgery)
Sharma, 2015, United Kingdom[45]	Retrospective chart review	Neonates and infants aged 15 to 178 days diagnosed with tongue-tie during June 2013 to July 2014 (n = 42 participants, of 54 eligible)	Unclear	Surgical frenotomy (n = 36, 86%)	Support from infant feeding coordinator (no surgery) (n = 6, 14%)	Infant Breastfeeding Assessment Tool scores pre and post-intervention Mother's perceptions of breastfeeding improvement at one month; Follow-up = 1 month

[a] The method of randomization was unclear and only briefly mentioned in the abstract of the report
[b] Excluding patients with congenital abnormalities in the craniofacial region, abnormal mental development, and difficulty feeding not attributable to tongue-tie
[c] Information about parental perceptions of the quality of service at the tongue-tie clinic was presented but is not summarized within this report
[d] Excluding patients with perinatal complications, craniofacial anomalies, visible genetic syndrome

Appendix 3: Study Overlap between Systematic Reviews

Table A3. Overlap in Included Studies between Systematic Reviews

Study Author, Publication Year, Study Type	Francis 2015[39]	Francis 2015[44] AHRQ	Ito 2014[40]
Primary Clinical Studies			
Amir 2005 (CS)	•	•	•
Argiris 2011 (CS)	•	•	•
Ballard 2002 (CS)	•	•	•
Berg 1990 (CR)		•	
Berry 2012 (RCT)	•	•	
Blenkinsop 2003 (CS)	•		
Buryk 2011 (RCT)	•	•	
Choi 2011 (CS)		•	
Chu 2009 (CR)		•	
Cunha 2008 (CR)		•	
Dave 2013 (CS)		•	
Dollberg 2006 (RCT)	•	•	
Dollberg 2011 (NRS)			
Dollberg 2014 (CS)	•	•	
Edmunds 2013 (CS)	•		
Emond 2014 (RCT)	•	•	
Finigan 2014 (CS)	•	•	•
Fiorotti 2004 (CS)		•	
Fleiss 1990 (CR)		•	
Geddes 2008 (CS)	•	•[a]	•
Godley 1994 (CS)		•	
Good 1987 (CR)		•	
Griffiths 2004 (CS)	•	•	•
Heller 2005 (RCT)		•	
Hogan 2005 (RCT)	•	•	
Hong 2010 (CS)	•	•	
Huggins 1990 (CR)		•	
Isaiah 2013 (CR)		•	
Khoo 2009 (CS)	•	•	•
Klockars 2009 (CS)	•	•	
Lalakea 2003 (CS)		•	
Lin 2009 (CR)		•	
Marchesan 2012 (CS)		•	
Marmet 1990 (NRS)			
Masaitis 1996 (CS)	•	•	•
Mathewson 1966 (CR)		•	
Messner 2002 (CS)		•	
Mettias 2013 (CS)	•	•	
Miranda 2010 (CS)	•		•
Nicholson 1991 (CR)		•	
O'Callahan 2013 (CS)	•		
One unpublished thesis		•	
Opara 2012 (CR)		•	
Puthussery 2011 (CS)		•	
Reddy 2014 (CR)		•	
Ridgers 2009 (CS)	•		•
Riskin 2014 (CS)	•	•	
Rose 2014/5 (CS)	•	•	
Santos Tde 2012 (CR)		•	
Sethi 2013 (CS)	•		
Sirinoglu 2013 (CR)		•	

Table A3. Overlap in Included Studies between Systematic Reviews

Study Author, Publication Year, Study Type	Francis 2015[39]	Francis 2015[44] AHRQ	Ito 2014[40]
Srinivasan 2006 (CS)	•		•
Steehler 2012 (NRS)	•	•	•
Toner 2014 (CS)	•	•	
Tuli 2010 (CR)		•	
Wallace 2006 (CS)	•	•	
Walls 2014 (RCT)		•	
Yeh 2008 (CS)		•	
Guidelines			
NICE Guideline (2005)			•
Academy of Breastfeeding Medicine Guideline			•
Canadian Paediatric Society Guideline (2011)			•

[a]Double counted

Appendix 4: Critical Appraisal of Included Publications

Table A4: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR[19]

AMSTAR Item		Francis, 2015[39]	Ito, 2014[40]
Was a priori design provided?		⊕	X
Was there duplicate study selection and data extraction?	Selection	⊕	?
	Extraction	⊕	?
Was a comprehensive literature search performed?		⊕	⊕
Was the status of publication (i.e., grey literature) used as an inclusion criterion?		⊕	⊕
Was a list of studies (included and excluded) provided?	Included	⊕	⊕
	Excluded	⊕	X
Were the characteristics of the included studies provided		⊕	⊕
Was the scientific quality of the included studies assessed and documented?		⊕	⊕
Was the scientific quality of the included studies used appropriately in formulating conclusion?		⊕	⊕
Were the methods used to combine the findings of studies appropriate?		N/A	X
Was the likelihood of publication bias assessed?		X	X
Was the conflict of interest included?		⊕	⊕

Legend: ⊕ = Yes, **X** = No, **?** = Unclear

Table A5: Strengths and Limitations of Primary Clinical Studies using Downs and Black[20]

Downs and Black Item	Randomized Controlled Trials	Non-Randomized Studies			
	Yousefi, 2015[41]	Braccio, 2016[42]	Pransky, 2015[44]	Martinelli, 2015[43]	Sharma, 2015[45]
Reporting					
Is the hypothesis/aim/objective of the study clearly described?	⊕	⊕	⊕	⊕	⊕
Are the main outcomes to be measured clearly described in the Introduction or Methods section?	⊕	X	X	⊕	⊕
Are the characteristics of the patients included in the study clearly described?	⊕	X	X	X	X
Are the interventions of interest clearly described?	⊕	X	⊕	⊕	⊕
Are the distributions of principal confounders in each group of subjects to be compared clearly described?	X	X	X	X	X
Are the main findings of the study clearly described?	X	X	⊕	X	⊕
Does the study provide estimates of the random variability in the data for the main outcomes?	⊕	⊕	X	⊕	⊕
Have all important adverse events that may be a consequence of the intervention been reported?	X	X	X	X	X
Have the characteristics of patients lost to follow-up been described?	N/A	X	N/A	X	N/A
Have actual probability values been reported for the main outcomes?	⊕	⊕	N/A	⊕	⊕
External Validity					
Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	X	X	X	X	X
Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	?	X	⊕	?	⊕

Table A5: Strengths and Limitations of Primary Clinical Studies using Downs and Black[20]

Downs and Black Item	Randomized Controlled Trials	Non-Randomized Studies			
	Yousefi, 2015[41]	Braccio, 2016[42]	Pransky, 2015[44]	Martinelli, 2015[43]	Sharma, 2015[45]
Were the staff, place, and facilities where the patients were treated, representative of the treatment the majority of patients receive?	X	X	X	X	?
Internal Validity – Bias					
Was an attempt made to blind study subjects to the intervention they have received?	X	X	X	X	X
Was an attempt made to blind those measuring the main outcomes of the intervention?	⊕	X	X	X	X
In trials and cohort studies do the analyses adjust for different lengths of follow-up of patients or in case-control studies is the time period between the intervention and outcome the same for cases and controls?	⊕	X	⊕	⊕	⊕
Were the statistical tests used to assess the main outcomes appropriate?	X	X	N/A	X	⊕
Was compliance with the intervention/s reliable?	⊕	⊕	⊕	⊕	⊕
Were the main outcome measures used accurate (valid and reliable)?	X	X	X	⊕[a]	⊕[a]
Internal Validity – Confounding					
Were the patients in different intervention groups or were the cases and controls recruited from the same population?	⊕	⊕	⊕	⊕	⊕
Were study subjects in different intervention groups or were the cases and controls recruited over the same period of time?	⊕	⊕	⊕	⊕	⊕
Were study subjects randomized to intervention groups?	⊕	N/A	N/A	N/A	N/A
Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?	?	N/A	N/A	N/A	N/A
Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	X	X	X	X	X
Were losses of patients to follow-up taken into account?	N/A	X	N/A	N/A	N/A
Power					
Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?	?	?	?	?	?
Additional Critical Appraisal Points					
Was conflict of interest mentioned?	⊕	⊕	⊕	⊕	?

[a]For select but not all outcomes

Appendix 5: Main Study Findings and Author's Conclusions

Table A6: Summary of Findings of Included Systematic Reviews

Outcome	Frenectomy Group	Comparator	Effect Estimate	Author's Conclusions or Interpretation	Considerations
Francis, 2015[4,39]					
	Frenotomy	Sham Surgery			
Breastfeeding Effectiveness					
Subjective Self-Reported Measures					
Maternally reported improvement in breast feeding	96%	LC: 3%	NR	A significantly higher proportion of infants had improved feeding within 48 hours in the frenectomy versus control group[50]	Study suffered from unclear randomization, lack of blinding, absence of longer-term follow-up data, and patient crossover after 48 hours in control group
	78%	47%	p = <0.02	Self-reported breastfeeding improvements in a greater proportion of frenectomy group than comparator immediately after intervention[27]	
	80.4%	NI: N/A	N/A	The majority of mothers surveyed reported improved ability to feed[35]	Study was rated as poor quality; not all participants agreed to follow-up assessment
Long-term follow-up	• One RCT[27] reported that 92% of mothers reported improved feeding, with 56% reporting complete resolution at 3 months; 65% of infants were being breastfed at 3 months, and 51% were still breastfeeding at 4.5 months; no differences between groups reported • One RCT[28] reported no difference between groups in breastfeeding effectiveness at 2 weeks follow-up • One RCT[30] reported no differences in LATCH score at 8 weeks				
Breastfeeding continuation (%), mean no. of months	82.9%, 7.09	NI: 66.7%, 6.28 months	NR	Breastfeeding was continued in a numerically higher proportion of cases for a longer duration in the frenectomy group versus no intervention;[35] Having a procedure earlier	Outcome was assessed as a secondary outcome

Table A6: Summary of Findings of Included Systematic Reviews

Outcome	Frenectomy Group	Comparator	Effect Estimate	Author's Conclusions or Interpretation	Considerations
				(first week of life) than later did not impact the duration of breastfeeding	
Discontinuation of breastfeeding due to pain (%)	17.1%	NI: 33.3%	NR	Discontinuation due to pain occurred in a smaller proportion of mothers in the frenectomy group versus no intervention[35]	
Breastfeeding Self-Efficacy Scale-Short Form (BSES-SF), median (IQR)[30]	9 (1.8 to 12.3)	NI: 1 (-4 to 7.5)	p = 0.0002	Significant improvement in BSES-SD score at 5 days post-intervention in frenotomy group	At 5 to 8 days there was no significant difference between groups and by 8 weeks both groups were similar in overall improvement; however, this is confounded by a substantial number of patients crossing over to receive frenotomy
HATLFF Score, median (IQR)	4.5 (3.3 to 6)	NI: 0 (0 to 2.3)	p <0.001	Significant improvement in HATLFF score at 5 days post-intervention in treatment group	
Objective Assessment					
IBFAT Score, median	11.6 ± 0.81	8.07 ± 0.86	p = 0.026	Observer interpreted breastfeeding effectiveness based on IBFAT score was improved in frenectomy group immediately after surgery; but no different at 2 week follow-up[28]	
	0 (IQR = -1.8 to 1.0)	NI: 0 (IQR = 0 to 1)	p = 0.36	No significant difference in IBFAT score between groups at 5 days post-procedure[30]	Many mothers in control group crossed over to receive frenotomy before outcomes were assessed

Table A6: Summary of Findings of Included Systematic Reviews

Outcome	Frenectomy Group	Comparator	Effect Estimate	Author's Conclusions or Interpretation	Considerations
Score adapted from LATCH and IBFAT, (% improvement)[27]	13/26 (50%)	12/30 (40%)	NR	No difference in improvement observed between groups immediately after intervention	
LATCH score[30]	1 (IQR = 0 to 2)	NI: 1 (IQR = 0 to 2)	p = 0.36	No difference in improvement in LATCH scores 5-days post-intervention[30]	Many mothers in control group crossed over to receive frenotomy before outcomes were assessed
Feeding Sequelae					
Improvement in feeding problems[50] n(%)	8(100)	0(0)	NR	In a group of children with a large proportion of major problems with dribbling and excess gas, mother's reported improved feeding in patients who received the procedure but not those that did not	Lots of crossover to receive procedure in usual care group after randomization
Likert scale for eating difficulty at 3 years	NR	NR	NR	Frenotomy group performed better on parent-reported scale assessing ability to clean teeth with tongue, lick outside of lips, and eat ice cream compared to patients with ankyloglossia who did not receive the procedure, but not patients without ankyloglossia (p<0.001 for all criteria)[59]	Study classified as poor quality; p-values reported without reporting the averages or measures of variability, reliability unclear
Number of breastfeeding sessions[55]			p <0.0001	At 2 weeks post-procedure the number of breastfeeding	Case series

Table A6: Summary of Findings of Included Systematic Reviews

Outcome	Frenectomy Group	Comparator	Effect Estimate	Author's Conclusions or Interpretation	Considerations
				sessions decreased from pre-procedure frequency	
Bottle feeding supplementary sessions[55]			p < 0.001	At 2 weeks post-procedure the number of bottle feeding supplementary sessions were decreased from pre-procedure frequency	Case series
Nipple Pain					
Montreal Pain Questionnaire (MPQ-SF)	4.9 ± 1.46	13.5 ± 1.5	p < 0.001	One RCT[28] reported significant immediate improvement in nipple pain (maternally reported) in frenectomy patients versus sham surgery), which was maintained at 4 weeks follow-up	Many mothers in control group crossed over to receive frenotomy before outcomes were assessed
Maternal pain scores (scale unspecified)[27]	-2.5 ± 1.9	-1.3 ± 1.5	p = 0.013	The two other RCTs found no differences in maternally reported nipple pain between groups immediately and 5-days post procedure[27,30]	
Change in maternal pain (VAS), median (IQR)[30]	At 5 days: -2 (-3 to 0.4) At 8 weeks: -2 (-3 to -1)	NI: At 5 days:-1 (-13.5 to 1) At 8 weeks: -2 (-3.5 to -0.6)	At 5 days: NS At 8 weeks: p = 0.83		Another study[29] assessed maternal breastfeeding pain or nipple trauma using a VAS and LATCH scores but did not present comparative results; therefore, results were not presented in the SR
Speech Outcomes or Social Concerns related to Tongue Mobility					
All findings were regarding older patients ages 3 and up, and may not be relevant to the neonatal and infant population of interest. Findings can be found on page 27 to 34 of the main report[4]					
Harms					
Harms were reported by 46 studies including comparative studies, case series, and case reports					Method of

Table A6: Summary of Findings of Included Systematic Reviews

Outcome	Frenectomy Group	Comparator	Effect Estimate	Author's Conclusions or Interpretation	Considerations

A large number of studies (n = 17) reported that no significant harms were observed or minimal harms
 	
Bleeding was the most frequent harm reported, and was described as minor and limited
 	
• Other infrequently reported harms included the need for reoperation (4%),[30] scarring (2.6%),[35]
• Healing slough requiring approximately 7 days to heal at the base of the frenulum was present in 64% of patients[30]
• Harms were described in one third of the 33 case series assessed
  ○ Minor bleeding occurred in 6 of 37 infants, and infant distress/pain was described in 2 of 36 infants in one case series[65]
  ○ Reoperation rates ranged from 0.1 to 27 percent, with the need for reoperation described by 5 case series
  ○ One case series reported mild scar tissue formation following frenuloplasty involving use of buccal mucosa grafts[66]
  ○ One case series reported no complications; however two patients reported pain, and one patient reported bleeding following laser frenectomy[60]
• 15 case reports collectively reported 2 cases of surgical site infection, three cases of reoperation, four cases of swelling and pain, and one case of post-surgical mucous cyst
  ○ One article reported two cases of hemorrhagic shock following frenotomy in Nigeria when performed by a traditional birth attendant and an untrained community health worker[61]
					collecting harms data was unclear for most studies

Ito, 2014[40]					
Breastfeeding Efficacy					
	Frenotomy	Placebo			
Overall breastfeeding improvement evaluated by mother, n = 2 studies	40/47	15/50	Pooled RR = 2.88 (95% CI = 1.82 to 4.57), I^2 = 90%	Meta-analysis indicated a greater likelihood of breastfeeding improvement in the frenotomy group versus placebo Significant improvement in overall assessment of breast-feeding observed by mothers in the frenotomy group	Greater incremental improvements observed in the non-blinded study[27] versus the non-blinded study[50] Sucking and latch difficult to assess independently from other outcomes as they were combined as maternal subjective outcome measures
	After	Before			
LATCH score, n = 2 studies	NR/51	NR/51	Pooled MD = 2.07 (95% CI = 1.64 to 2.49), I^2 = 81%	Meta-analysis of two observational studies supported the effectiveness of frenotomy	

Table A6: Summary of Findings of Included Systematic Reviews					
Outcome	Frenectomy Group	Comparator	Effect Estimate	Author's Conclusions or Interpretation	Considerations
				In observational studies, sucking/latch immediately improved from 57 to 92% after frenotomy[22,54-57]	
Nipple Pain					
	After	Before			
Nipple pain, n = 3 studies	NR/123	NR/123	Pooled MD = -5.10 (95% CI = -5.60 to -4.59), I^2 = 83%	Meta-analysis of three observational studies demonstrated a reduction in nipple pain after the procedure Of three RCTs, two showed a significant improvement in pain[28,29] where there was no significant difference in pain scores in the other[27] Five observational studies[52,53,55,57,58] reported on nipple pain, with four[16,52,53,57] reporting a significant improvement in pain following frenectomy	The RCTs used different outcome measures used (visual analogue scale in two studies, McGill pain questionnaire in 1 study)
Milk Supply, Continuation of Breastfeeding and Growth					
Milk supply/milk production, n = 1 study				Significant increase in milk transfer (mL/min) ($p < 0.01$) and 24 hour milk production measured in six mothers ($p = 0.035$)[52]	
Continuation of breast feeding, n = 8 studies				Continuation rate ranged from 43% to 78% at 3 month follow-up. Author's commented that	All studies uncontrolled [22,27,35,50,51,53,54,56]

Table A6: Summary of Findings of Included Systematic Reviews					
Outcome	Frenectomy Group	Comparator	Effect Estimate	Author's Conclusions or Interpretation	Considerations
				this is substantially higher than the UK national average of 29% at 4 months of age	
Weight gain, n = 1 study	56 ± 2.4	41 ± 2.5 (Before surgery)	MD = 15 (95% CI = 14.05 to 15.95)	Neonates gained significant weight by 15 centiles 2 weeks post frenotomy compared to pre-surgery weight ($p < 0.0001$)[55]	
Harms					
• "Minor bleeding usually readily controlled by applying gentle pressure to the site with a sponge." (page 501)[40] • The majority of includes articles did not report any major adverse events[22,27-29,35,50-58,67,68]					
Positions or Recommendations					
Guideline, guidance and position statements	• The ABM, based on observational evidence up to 2002 reported that, "although conservative management of tongue-tie is usually sufficient, frenotomy may be considered appropriate for partial ankyloglossia and, if necessary, the procedure should be performed by an experienced physician or pedodontist."[63] • NICE issued guidance in 2005 reported that "current evidence suggests there are no major safety concerns about division of ankyloglossia, and the procedure can improve breast-feeding." – however, noted that evidence was limited[62] • The Canadian Pediatric Society issued a position statement in 2011 which noted that "frenotomy is not commonly recommended, but if an association between significant tongue-tie and major breast-feeding problems is clearly identified and surgical intervention is deemed necessary, frenotomy should be performed by a clinician experienced with the procedure."[2]				Many of these statements are based on older evidence or solely on clinical opinion and a non-systematic process of evidence review No guidelines based on new evidence including several RCTs have not been issued

ABM = Academy of Breastfeeding Medicine; IBFAT = Infant Breast Feeding Assessment Tool; LATCH = latch, audible sw allowing, type of nipple, comfort and hold score; LC = lactation consultant support; NI = no intervention; NICE = The national Institute for Health and Care Excellence; NR = not reported; NRS = non-randomized study; RCT = randomized controlled trial

Table A7: Summary of Findings of Included Primary Clinical Studies

Outcome	Frenectomy Group	Comparator	Effect Estimate	Author's Conclusions or Interpretation	Considerations
Yousefi, 2015[41]					
Effectiveness Outcomes					
	Simple Release, n = 9	Z-plasty, n = 18			
Breastfeeding score[a]	2.33	2.66	p = 0.253	Both simple release and Z-plasty had a statistically significant impact on improving breastfeeding (p <0.0001), but there were no significant differences between groups	
Jaw locking (better latching)	2.63	2.79	p = 0.621	While there was an improvement in jaw locking resulting in better sucking in breast-feeding children (p < 0.001), there was no difference between surgical methods	
Breast pain (mean pain reduction)	5.71	6.37	p = 0.39	Both methods resulted in a significant reduction in breast pain (p <0.0001), but there were no significant differences between groups	
Articulation,[b] mean	1.94	3	p = 0.001	Both methods resulted in improvement in articulation, with a statistically greater improvement observed in the Z-plasty group	Children of speaking age, unlikely that these findings apply to neonates and infants
	n = 20	n = 11			
Effect on improvement of tongue movement (Hazelbaker's functional scoring assessment), mean	2.10	2.91	p = 0.001	A significant improvement in tongue mobility was observed for both groups, with a significantly greater improvement in the Z-plasty group	Unclear if these patients were neonates or infants, generalizability unclear
Tongue release and elongation, mean (SD) (mm)	6.93 (NR) before; 10.44 (3.79)	6.8 (NR) before; 17.56 (4.48)	p <0.001	Significant difference in tip to base distance after	

Table A7: Summary of Findings of Included Primary Clinical Studies

Outcome	Frenectomy Group	Comparator	Effect Estimate	Author's Conclusions or Interpretation	Considerations
	after	after		surgery, which was greater in the Z-plasty group	
Parent satisfcation[c]	8.6 (2.29)	10 (0)	p = 0.005	Z-plasty resulted in greater parent satisfaction with the procedure versus simple release	
Adverse Events					
Minor hemorrhage not requiring surgical intervention, n	0	1	NR		
Adhesion requiring reoperation, n	1	0	NR		
Braccio, 2016[42]					
	Before frenotomy	After frenotomy			
Effectiveness Outcomes					
Rate of exclusive breastfeeding, (n, %)	58 (36.7%)	85 (53.8%) at 48 hours 71 (44.9%) at follow-up[d]	OR = 4.857 (95% CI = 2.120 to 12.983)	Significant increase in exclusive breastfeeding from before frenotomy to 48 hours post-surgery	Increase in exclusive breastfeeding seen at 48 hours was reduced at follow-up Moderate reduction in formula milk use observed at 48 hours was reversed for an overall increase at follow-up No statistical analysis was conducted on before-and-after changes at follow-up time as authors thought it may be influenced by other factors (e.g., weaning, return to work, lack of family or community support) for which data was not collected
Formula milk use, (n, %)	52 (32.9%)	45 (28.5%) at 48 hours 80 (50.6%) at follow-up[d]	OR = 0.632 (95% CI = 0.280 to 1.370)	No significant difference in formula milk use from before frenotomy to 48 hours post-surgery	
Breastfeeding related problems (e.g., breast pain, cracked nipples), (n, %)	118 (79.2%)	36 (24.5%) at 48 hours 3 (2.7%) at follow-up[d]		Rate of reported breastfeeding problems showed a decrease after frenotomy at 48 hours and follow-up	Note this is a composite of problems for woman (e.g., breast pain and cracked nipples), frequent/prolonged

Table A7: Summary of Findings of Included Primary Clinical Studies

Outcome	Frenectomy Group	Comparator	Effect Estimate	Author's Conclusions or Interpretation	Considerations
					feeds, shallows latch, fussiness and restlessness and poor weight gain; Rate of breastfeeding problems at time of follow-up not analyzed as authors expected that at 4 months of age women experiencing major problems would be unlikely to continue breastfeeding and may be attributable to other factors
Frequent/prolonged feeds, (n, %)	116 (77.9%)	44 (29.9%) at 48 hours; 8 (7.1%) at follow-up[d]	OR = 0.027 (95% CI = 0.003 to 0.101)	Significantly lower odds of women reporting frequent or prolonged feeds (time point of observation not specified)	
Shallow latch, (n, %)	118 (79.2%)	34 (23.1%) at 48 hours; 7 (6.2%) at follow-up[d]	p < 0.0001	Significant decrease in the rate of shallow latch at 48 hours	
Fussiness/restlessness, (n, %)	102 (68.5%)	36 (24.5%) at 48 hours; 6 (5.3%) at follow-up[d]	P < 0.0001	Significant reduction in rate of women reporting fussiness of infant at the breast after frenotomy (time period of observation not specified)	
Complications					
Adverse events	No occurrence of major bleeding, infection or ulceration reported				
Persistent breastfeeding problems and requirement for reoperation	5 infants returned to clinic with persistent breastfeeding problems: • 1 re-attended four times and required 3 further procedures • 2 re-attended once required a second procedure • 1 re-attended twice and required a second procedure				
Pransky, 2015[44]					
Effectiveness Estimates					

Improvement after breastfeeding (%)	• Anterior ankyloglossia: 78% improved
	  ○ 61% significant
	  ○ 13% moderate
	  ○ 3% mild
	  ○ 19% no change
					No statistical tests conducted for differences in degree of improvement

Table A7: Summary of Findings of Included Primary Clinical Studies

Outcome	Frenectomy Group	Comparator	Effect Estimate	Author's Conclusions or Interpretation	Considerations
	○ 4% could not determine[e] • Posterior ankyloglossia: 91% improved ○ 23% significant improvement ○ 55% reported moderate improvement ○ 13% mild improvement ○ 7% no change ○ 2% could not determine[e] • Anterior ankyloglossia and upper-lip tie: 91% improved ○ 76% significant improvement ○ 9% moderate improvement ○ 6% mild improvement ○ 6% no change ○ 3% could not determine[e] • Posterior ankyloglossia and upper-lip tie: 85% improved ○ 61% significant improvement ○ 18% moderate improvement ○ 6% mild improvement ○ 15% no change ○ 0% could not determine[e]				between groups or to quantify within group changes
Adverse Events	No complications reported after the procedure in any of the groups				Complications and long-term follow-up were self-reported not assessed
Martinelli, 2015[43]					
	Infants with tongue-tie undergoing frenotomy	Infants without tongue-tie			
Effectiveness Outcomes					
Average number of sucks in each one of the three first groups of sucking before surgery at 30 days of age	19.36 ± 13.02	55.76 ± 21.00	p = 0.005	Before the procedure, infants in the frenotomy group had significantly lower average number of sucks than the control group without tongue-tie	
Average number of sucks in each one of the three first groups of sucking after surgery at 75 days of age	53.76 ± 7.99	54.50 ± 20.88	p > 0.05	No significant difference in average number of sucks between groups	Measurements for control group made at 30 days, not 75 days
Pause length measurement before surgery (seconds) at 30 days	6.14 ± 2.47	3.00 ± 0.63	p < 0.001	Significantly higher pause length in frenotomy group versus controls before surgery	
Pause length measurement after surgery (seconds) at 75 days	3.88 ± 0.88	3.30 ± 0.67	p > 0.05	No significant difference in pause length between groups at follow-up	Measurements for control group made at 30 days, not 75 days
	Before surgery	After surgery			
Average number of sucks in each one of the three first	19.36 ± 13.02	53.76 ± 7.99	p < 0.001	The average number of sucks	

Table A7: Summary of Findings of Included Primary Clinical Studies

Outcome		Frenectomy Group	Comparator	Effect Estimate	Author's Conclusions or Interpretation	Considerations
groups of sucking after surgery					was significantly increased in the frenotomy group after surgery; where it remained similar in the control group ($p > 0.05$, data not shown)	
Pause length measurement (seconds)		6.14 ± 2.47	3.88 ± 0.88	$p = 0.013$	The average pause length was significantly reduced in the frenotomy group after surgery; where it remained similar in the control group ($p > 0.05$, data not shown)	
		Overall Observations				
Breastfeeding Symptoms		The rate of problems related to duration of feedings, sleep between feedings, sleep during breastfeeding, sleepiness during breastfeeding, pauses between sucking, nipple chewing, strength of suck, tongue clicking, latch, and maternal nipple pain were numerically reduced at the final assessment (75 days) compared to pre-surgery (30 days) rates in the frenotomy group			Based on qualitative assessment of breastfeeding, the rate of reported symptoms related to breastfeeding problems were reduced after frenotomy	No statistical tests conducted to assess differences in before and after values; Measurements are subjective and based on questionnaire data; No measurements made in control group at follow-up preventing comparisons between groups
Sucking/Swallowing/Breathing and Coordination		The rate of problems related to sounds during swallowing, choking, hiccups, cough, and regurgitation were numerically reduced at the final assessment (75 days) compared to pre-surgery (30 days) rates in the frenotomy group				
Sharma, 2015[45]						
		Frenotomy (n = 36)	Support from Infant Feeding Coordinator (n = 6)			
Effectiveness Outcomes						
Maternal reported improvement in breastfeeding, (n,%)	Overall	29 (81%)	1 (17%)	$p = 0.0084$	Significantly higher proportion of mothers reported improved breastfeeding in the frenotomy group	Group sample sizes imbalanced, control group too small to detect a difference
	Children < 30 days old	16/17 (94%)	N/A	$p = 0.092$	No significant differences in the rate of reported improvement in	Unclear if there was appropriate power to detect a difference;
	Children ≥	13/19	N/A			

Table A7: Summary of Findings of Included Primary Clinical Studies

Outcome		Frenectomy Group	Comparator	Effect Estimate	Author's Conclusions or Interpretation	Considerations
	30 days old	(68%)			breastfeeding by mothers, between older and younger children	Noted in the discussion that the study indicates a higher probability of improvement, however the non-significant results suggest no difference
		Pre-intervention	Post-intervention			
IBFAT score	Frenotomy group	3.33 ± 1.51	9.19 ± 2.44	p = 0.0001	Significant improvement in IBFAT score was observed in the frenotomy group after the intervention, but not in the control group upon second assessment	Does not speak to the time spent breastfeeding – or longer term outcomes Telephone survey (selection bias)
	Control group	4.17 ± 0.75	6.00 ± 1.73	p = 0.16		

IBFAT= Infant Breastfeeding Assessment Tool

[a]0 = no change, 1 = improved, 2 = good improved, 3 = full resolution of feeding problems;

[b]1 = no change, 2 = good, 3 = better, 4 = best based on words involving 'D', 'T', and 'N'T before and after surgery chosen in consultation with speech pathologist and "they best assess the need to bring the tongue forward and upward as required in the Persian language"[41]

[c]Score of 1 to 10

[d]Median = 4 months

[e]As child was asleep or bottle fed following procedure

Appendix 6: Additional References of Potential Interest

Ongoing or Unpublished Systematic Reviews

O'Shea J, Foster J, O'Donnell C, Breathnach D, Jacobs S, Todd D, et al. Frenotomy for tongue-tie in newborn infants [Cochrane protocol] [Internet]. York, United Kingdom: Centre for Reviews and Dissemination; 2015 Mar 31. [cited 2016 May 27]. Available from: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015018984

Allepuz A, Ramos F, Pons J. Ankyloglossia, breastfeeding and frenotomy effectiveness: a systematic review of the literature [Internet]. York, United Kingdom: Centre for Reviews and Dissemination; 2012 Apr 12. [cited 2016 May 27]. Available from: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42011001530

Hosida T, Souza J, Cunha RF, Pessan JP, Delbem A. Comparison of laser and conventional technique after labial frenectomy: a systematic review [Internet]. York, United Kingdom: Centre for Reviews and Dissemination; 2016 Nov 4. [cited 2016 May 27]. Available from: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015027665

Ongoing Clinical Studies

Patients with Tongue-Tie and Concomitant Lip-Tie

Prospective evaluation of lingual frenotomy in newborns with simultaneous lip tie for the relief of breastfeeding pain. 2015 Dec [cited 2016 May 27]. In: ClinicalTrials.gov [Internet]. Bethesda (MD): U.S. National Library of Medicine; 2000 - . Available from: https://clinicaltrials.gov/ct2/show/NCT02141243?term=frenotomy&rank=1 Identifier: NCT02141243.

Breastfeeding improvement following tongue-tie and lip-tie release. 2016 Dec [cited 2016 May 27]. In: ClinicalTrials.gov [Internet]. Bethesda (MD): U.S. National Library of Medicine; 2000 - . Available from: https://clinicaltrials.gov/ct2/show/NCT02642133?term=frenotomy&rank=6 Identifier: NCT02642133.

Use of Topical or Oral Pain Medication during Frenectomy

Use of topical benzocaine for analgesia in lingual frenotomy of the newborn. 2012 Aug [cited 2016 May 27]. In: ClinicalTrials.gov [Internet]. Bethesda (MD): U.S. National Library of Medicine; 2000 - . Available from: https://clinicaltrials.gov/ct2/show/NCT01274247?term=frenotomy&rank=3 Identifier: NCT01274247.

Pain associated with neonatal frenotomy. 2014 Dec [cited 2016 May 27]. In: ClinicalTrials.gov [Internet]. Bethesda (MD): U.S. National Library of Medicine; 2000 - . Available from: https://clinicaltrials.gov/ct2/show/NCT01914250?term=frenotomy&rank=5 Identifier: NCT01914250