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Marian Knight,[1*] Rema Ramakrishnan,[1] Svetlana Ratushnyak,[1] Oliver Rivero-Arias,[1] Jennifer Bell,[1] Ursula Bowler,[1] Phyll Buchanan,[2] Claire Carter,[3] Christina Cole,[1] Oliver Hewer,[1] Madeleine Hurd,[1] Andy King,[1] Ed Juszczak,[4] Louise Linsell,[1] Anna-May Long,[5] Linda Mottram,[1] David Murray,[1] Sam Oddie,[6] Maria Quigley,[1] Victoria Stalker,[1] Kayleigh Stanbury,[1] Richard Welsh[1] and Pollyanna Hardy[1] on behalf of the FROSTTIE Trial Collaborative Group

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Abstract

Frenotomy with breastfeeding support versus breastfeeding support alone for infants with tongue-tie and breastfeeding difficulties: the FROSTTIE RCT

Marian Knight[1*] Rema Ramakrishnan[1] Svetlana Ratushnyak[1] Oliver Rivero-Arias[1] Jennifer Bell[1] Ursula Bowler[1] Phyll Buchanan[2] Claire Carter[3] Christina Cole[1] Oliver Hewer[1] Madeleine Hurd[1] Andy King[1] Ed Juszczak[4] Louise Linsell[1] Anna-May Long[5] Linda Mottram[1] David Murray[1] Sam Oddie[6] Maria Quigley[1] Victoria Stalker[1] Kayleigh Stanbury[1] Richard Welsh[1] and Pollyanna Hardy[1] on behalf of the FROSTTIE Trial Collaborative Group

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Background: Tongue-tie can be diagnosed in 3–11% of babies, with some studies reporting almost universal breastfeeding difficulties, and others reporting very few feeding difficulties that relate to the tongue-tie itself, instead noting that incorrect positioning and attachment are the primary reasons behind the observed breastfeeding difficulties and not the tongue-tie itself. The only existing trials of frenotomy are small and underpowered and/or include only very short-term or subjective outcomes.

Objective: To investigate whether frenotomy is clinically and cost-effective to promote continuation of breastfeeding at 3 months in infants with breastfeeding difficulties diagnosed with tongue-tie.

Design: A multicentre, unblinded, randomised, parallel group controlled trial.

Setting: Twelve infant feeding services in the UK.

Participants: Infants aged up to 10 weeks referred to an infant feeding service (by a parent, midwife or other breastfeeding support service) with breastfeeding difficulties and judged to have tongue-tie.

Interventions: Infants were randomly allocated to frenotomy with standard breastfeeding support or standard breastfeeding support without frenotomy.

Main outcome measures: Primary outcome was any breastmilk feeding at 3 months according to maternal self-report. Secondary outcomes included mother's pain, exclusive breastmilk feeding, exclusive direct breastfeeding, frenotomy, adverse events, maternal anxiety and depression, maternal and infant NHS health-care resource use, cost-effectiveness, and any breastmilk feeding at 6 months of age.

Results: Between March 2019 and November 2020, 169 infants were randomised, 80 to the frenotomy with breastfeeding support arm and 89 to the breastfeeding support arm from a planned sample size of 870 infants. The trial was stopped in the context of the COVID-19 pandemic due to withdrawal of breastfeeding support services, slow recruitment and crossover between arms. In the frenotomy with breastfeeding support arm 74/80 infants (93%) received their allocated intervention, compared to 23/89 (26%) in the breastfeeding support arm. Primary outcome data were available for 163/169 infants (96%). There was no evidence of a difference between the arms in the rate of breastmilk feeding at 3 months, which was high in both groups (67/76, 88% vs. 75/87, 86%; adjusted risk ratio 1.02, 95% confidence interval 0.90 to 1.16). Adverse events were reported for three infants after surgery [bleeding (n = 1), salivary duct damage (n = 1), accidental cut to the tongue and salivary duct damage (n = 1)]. Cost-effectiveness could not be determined with the information available.

Limitations: The statistical power of the analysis was extremely limited due to not achieving the target sample size and the high proportion of infants in the breastfeeding support arm who underwent frenotomy.

Conclusions: This trial does not provide sufficient information to assess whether frenotomy in addition to breastfeeding support improves breastfeeding rates in infants diagnosed with tongue-tie.

Future work: There is a clear lack of equipoise in the UK concerning the use of frenotomy, however, the effectiveness and cost-effectiveness of the procedure still need to be established. Other study designs will need to be considered to address this objective.

Trial registration: This trial is registered as ISRCTN 10268851.

Funding: This project was funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment Programme (project number 16/143/01) and will be published in full in *Health Technology Assessment*; Vol. 27, No. 11. See the NIHR Journals Library website for further project information. The funder had no role in study design or data collection, analysis and interpretation. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

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List of abbreviations

aRR	adjusted risk ratio
BTAT	Bristol Tongue Assessment Tool
CACE	complier-average causal effect
CI	confidence interval
CTU	Clinical Trials Unit
CUA	cost-utility analysis
DMC	Data Monitoring Committee
EQ-5D-5L	EuroQol-5 Dimensions, five-level version
HRQoL	health-related quality of life
ICER	incremental cost-effectiveness ratio
IQR	interquartile range
ITT	intention to treat
NICE	National Institute for Health and Care Excellence
NPEU	National Perinatal Epidemiology Unit
PPI	patient and public involvement
QALDs	quality-adjusted life-days
QALYs	quality-adjusted life-years
RCT	randomised controlled trial
RR	risk ratio
SAE	serious adverse event
SD	standard deviation
SF-MPQ	Short Form McGill Pain Questionnaire
TSC	Trial Steering Committee

Plain language summary

Many mothers and babies experience difficulties in establishing breastfeeding. In some babies it is thought that their difficulties may be linked to a condition called tongue-tie, in which a piece of skin tightly joins the middle part of the underside of the tongue to the base of the baby's mouth. This can be treated by an operation to divide the tight part/skin in the middle of the underneath of the tongue.

We planned to carry out a trial of 870 babies to find out whether an operation together with breastfeeding support helps more mothers and babies with tongue-tie to continue breastfeeding until the baby is 3 months old compared to breastfeeding support on its own and whether the costs were different between the two groups of mothers and babies. We were only able to recruit 169 babies as the trial was stopped because of slow recruitment, changes to services in the COVID-19 pandemic and a high proportion of the babies in the breastfeeding support group going on to have an operation.

There were no differences in the rate of breastfeeding at 3 months between the babies in the group who had an operation straightaway and those in the group that had breastfeeding support alone, or had an operation later. More than four in every five babies in both groups were still breastmilk feeding at 3 months. Three babies who had an operation, around 1 in 50 babies, had a complication of the operation (bleeding, scarring or a cut to the tube that makes saliva).

Because of the small size of the study, we cannot say whether an operation to divide a tongue-tie along with breastfeeding support helps babies with tongue-tie and breastfeeding difficulties or has different costs. We will need to try different types of research to answer the question.

Scientific summary

Background

Breastfeeding difficulties have been associated with many factors, from a societal to an individual level. Tongue-tie can be diagnosed in 3–11% of babies, with the variation in reported prevalence thought to relate to the use of different diagnostic or severity criteria. Up to half of babies with tongue-tie are reported to have breastfeeding difficulties, but the reported proportion is highly variable. Some studies report almost universal difficulties, and others report very few feeding difficulties that relate to the tongue-tie itself, instead noting that incorrect positioning and attachment are the primary reasons behind the observed breastfeeding difficulties and not the tongue-tie itself. In a UK survey, it was noted that management of tongue-tie in infants with breastfeeding difficulties was therefore highly variable across the country. This is coupled with highly variable provision of breastfeeding support, which can range from minimal to expert and intensive, and using a variety of different models including peer supporter, midwife and health visitor.

A Cochrane review identified five prior randomised controlled trials (RCTs) of frenotomy including a total of only 302 infants. The trials are small and underpowered and/or include only very short-term or subjective outcomes, suggesting further robust evidence is needed. Hence there is considerable controversy regarding, not only the diagnosis and clinical significance, but also the management of tongue-tie. Current National Institute for Health and Care Excellence (NICE) guidance allows for the procedure, based on lack of safety concerns, but notes very limited evidence of efficacy. There is therefore a clear need for an assessment of the clinical- and cost-effectiveness of frenotomy for babies diagnosed with tongue-tie in the form of an adequately powered, pragmatic RCT, taking into account the diagnostic controversy and variation in practice.

Objective

To investigate whether frenotomy is clinically- and cost-effective to promote continuation of breastfeeding at 3 months in infants with breastfeeding difficulties diagnosed with tongue-tie.

Methods

Study design

The FROSTTIE trial was a multicentre, RCT conducted in 12 infant feeding services in England.

Participants

Inclusion criteria

- Any infant aged <10 weeks referred (by parent or other breastfeeding support service) to an infant feeding service with breastfeeding difficulties and judged to have tongue-tie, whose parent has given informed consent for participation.

Exclusion criteria

Infants were not eligible to enter the study if ANY of the following applied:

- Infant was older than 10 weeks.
- Infant had breastfeeding difficulties but was not judged to have tongue-tie.
- Infant was born at <34 weeks' gestation.
- Infant had a congenital anomaly known to interfere with breastfeeding, for example cleft palate, Down syndrome.
- Infant had a known bleeding diathesis.
- Infant had a frenotomy prior to recruitment.

Interventions

Infants were randomised to receive either a frenotomy with standard breastfeeding support or standard breastfeeding support without frenotomy.

Outcomes

Primary outcome

Any breastmilk feeding at 3 months according to maternal self-report, defined as follows:

- any breastmilk feeding in the 24 hours prior to the infant reaching 3 months of age.

Secondary outcomes

Mother's breastfeeding self-efficacy: measured using the Breastfeeding Self-Efficacy Scale – Short Form

Mother's pain while feeding during the previous 24 hours: measured using visual analogue scale of the Short Form McGill Pain Questionnaire, modified into a Likert-type scale

Amount of breastfeeding support used: measured by total number of contacts (whether face-to-face or virtual) with any breastfeeding supporter since the FROSTTIE procedure

Infant weight gain: measured as difference in weight for age *z*-scores between birth and 3 months of age

Infant postrandomisation weight gain: measured as difference in weight for age *z*-scores between baseline and 3 months of age

Exclusive breastmilk feeding: exclusive breastmilk feeding in the previous 24 hours

Exclusive direct breastfeeding: exclusive breastfeeding directly from the breast with no bottle feeds of expressed milk in the previous 24 hours

Age of child when s/he last received breastmilk: age when child last received breastmilk, to determine when and whether switch to exclusive formula feeding has occurred

Time spent breastfeeding in previous 24 hours: time in minutes/hours spent breastfeeding in previous 24 hours

Frenotomy in comparator group/repeat frenotomy/bleeding following frenotomy or frenulum tear/postprocedure adverse events (tongue cut, salivary duct damage)/maternal and infant NHS health-care resource use): measured by specific questions

Maternal anxiety and depression: dimension of EuroQol-5 Dimensions, five-level version (EQ-5D-5L)

Maternal health-related quality of life: as elicited by the EQ-5D-5L

Any breastmilk feeding at 6 months: according to maternal self-report: defined as any breastmilk feeding in the 24 hours prior to the infant reaching 6 months of age.

Process outcomes

The process outcomes for all infants included the Bristol Tongue Assessment Tool (BTAT) score by adherence status, reasons for non-adherence, and type of breastfeeding support.

Statistics and analysis plan

Sample size

It was assumed that a 10% absolute increase in the rate of breastfeeding represented the minimal clinically important difference that should be detectable by the trial; and breastfeeding rates will remain high in this motivated population. Thus assuming a breastfeeding rate of 70% in the control group and 80% in the intervention group, at 90% power with a 5% level of significance, and allowing for 5% loss to follow-up, with a further 5% increase to account for between-group contamination required a sample size of 870. Given the final sample size achieved with primary outcome data (n = 163), the study had 31% power to detect this difference, assuming the same control group rate.

Statistical analyses

Statistical analyses were carried out according to a pre-specified Statistical Analysis Plan finalised prior to unblinding. For the primary analysis for all primary and secondary outcomes infants were analysed in the groups to which they were randomly assigned [referred to as the intention-to-treat (ITT) population]. Demographic and clinical data were summarised with counts and percentages for categorical variables, means (standard deviations [SDs]) and medians (with interquartile or simple ranges) for continuous variables. For binary outcomes, risk ratios and confidence intervals (CIs) were calculated using log binomial regression or Poisson regression with a robust variance estimator. Continuous outcomes were analysed using linear and median (quantile) regression for normally distributed and skewed variables, respectively. Analyses were adjusted for stratification factors at randomisation where possible (centre, infant's age at randomisation and mother's parity). Two-sided statistical testing was performed throughout. A 5% level of statistical significance was used, and 95% CIs are presented.

Secondary analyses

Four planned secondary analyses were carried out:

1. A comparison of the characteristics and primary outcome by adherence status in the breastfeeding support arm.
2. An assessment of the impact of non-adherence to the randomised allocation using complier-average causal effect analysis.
3. A restricted per-protocol analysis, excluding participants who did not receive the allocated intervention as randomised.
4. An as-treated analysis, grouping participants according to the allocation they received.

Pre-specified subgroup analyses

Four planned subgroup analyses were carried out, examining the primary outcome in the following groups:

- infants aged <2 weeks versus ≥2 weeks at randomisation
- infants with BTAT score 4 or less versus 5–6 versus 7 or more at randomisation
- prior belief concerning frenotomy: likely to be beneficial versus uncertain versus unlikely
- recruited pre- or posttrial pause during the COVID-19 pandemic.

Economic evaluation

We conducted a within-trial cost-consequence analysis that assessed health-care resource utilisation, costs and benefits associated with frenotomy with breastfeeding support versus breastfeeding support only in mothers and their infants with breastfeeding difficulties and judged to have tongue-tie. In a secondary analysis, a cost-utility investigation was conducted to understand the potential value for money of frenotomy with breastfeeding support compared to no frenotomy.

Site monitoring

A monitoring plan for the trial, including responsibilities, was developed prior to the start of recruitment. In person monitoring of sites was carried out to identify barriers and facilitators to recruitment and the findings of the visits summarised to guide ongoing actions to enhance recruitment.

Results

Between March 2019 and November 2020, 169 infants were randomised, 80 to the frenotomy with breastfeeding support arm and 89 to the breastfeeding support arm from a planned sample size of 870 infants. The trial was stopped in the context of the ongoing COVID-19 pandemic due to withdrawal of breastfeeding support services, slow recruitment and crossover between arms. In the frenotomy with breastfeeding support arm 74/80 infants (93%) received their allocated intervention, compared to 23/89 (26%) in the breastfeeding support arm.

Characteristics of participants were similar between the two trial arms. Infants had a mean age of 3 weeks, 87% were born at ≥38 weeks' gestation, and they had a mean birthweight of 3439g. Overall 33% of infants had a BTAT score of 4 or less, 66% had exclusive breastmilk feeding in the previous 24 hours, and 40% had exclusive direct breastmilk feeding. Thirty-four per cent of infants had also received formula milk in the previous 24 hours.

Mothers were a mean of 32 years old, 94% were of white ethnicity, and 48% had a previous live birth. Only 8% were resident in the most deprived quintile of areas. Mothers reported a mean pain score of 4 out of 10 while feeding during the previous 24 hours and 42% had some anxiety or depression. More than half of women recruited to the trial believed a frenotomy would help their baby.

Primary outcome

Primary outcome data were available for 163/169 infants (96%). There was no evidence of a difference between the arms in the rate of breastmilk feeding at 3 months, which was high in both groups [67/76, 88% vs. 75/87, 86%; adjusted risk ratio (aRR) 1.02, 95% CI 0.90 to 1.16].

Secondary outcomes

As would be anticipated by the small size of the trial, there was no evidence of differences in any secondary outcomes comparing infants in the frenotomy with breastfeeding support arm to the breastfeeding support arm at 3 months.

Mother's breastfeeding self-efficacy: Median Breastfeeding Self-Efficacy Scale score 60.0 versus 56.5, adjusted median difference 0.3 (95% CI 5.2 to 5.8)

Mother's pain while feeding during the previous 24 hours: median 0 out of 10 versus 0, adjusted median difference −0.2 (95% CI 0.6 to 0.3)

Amount of breastfeeding support used: median 3 contacts versus 2, adjusted median difference −0.3 (95% CI −1.5 to 1.0)

Infant weight gain from birth: mean difference in weight for age *z*-score −1.1 versus −1.2, adjusted mean difference 0.17 (95% CI −0.60 to 0.95)

Infant postrandomisation weight gain: mean difference in weight for age *z*-score −1.0 versus −1.1, adjusted mean difference 0.10 (95% CI −0.83 to 1.03)

Exclusive breastmilk feeding: exclusive breastmilk feeding in the previous 24 hours 45/71 (63%) versus 50/75 (67%), aRR 0.92 (95% CI 0.61 to 1.39)

Exclusive direct breastfeeding: 38/71 (54%) versus 39/74 (53%), aRR 1.03 (95% CI 0.65 to 1.62)

Age of child when s/he last received breastmilk: not measurable due to high rates of continued breastfeeding

Time spent breastfeeding in previous 24 hours: median 3 hours versus 3 hours, adjusted median difference 0.1 (95% CI −1.1 to 1.2)

Frenotomy performed: 75/80 (94%) versus 65/89 (73%)

Maternal anxiety and depression: 29/73 (40%) versus 26/75 (35%), aRR 1.12 (95% CI 0.65 to 1.93)

Maternal health-related quality of life: mean [standard deviation (SD)]: 0.85 (0.18) versus 0.87 (0.12), adjusted mean difference 0.00 (95% CI −0.07 to 0.07)

Maternal and infant NHS health-care resource use: mean (SD) £497 (£854) versus £483 (£529), mean cost difference £21 (95% CI −£221 to £263)

Any breastmilk feeding at 6 months: 55/66 (83%) versus 60/71 (85%), aRR 0.98 (95% CI 0.84 to 1.14)

Adverse events occurred in three infants (one infant had bleeding, one infant had salivary duct damage, and the third infant had an accidental cut to the tongue and salivary duct damage). There were no other serious adverse events causally related to the intervention.

Pre-specified subgroup analyses

There were no notable differences between both the arms for any of the selected subgroups except that the rate of breastmilk feeding at 3 months appeared higher in the frenotomy with breastfeeding support arm compared to the breastfeeding support arm (92% vs. 83%) before the trial paused due to the COVID-19 pandemic. After the trial restarted the rate appeared higher in the breastfeeding support arm compared to the frenotomy with breastfeeding support arm (91% vs. 81%).

Economic evaluation

There were no statistically significant differences in health-care resource use, costs and benefits between the two groups. Given the current sample size to conduct the cost-effectiveness analysis and the number of infants in the breastfeeding support group receiving frenotomy, there is substantial uncertainty about whether frenotomy represents good value for money of NHS resources when compared to breastfeeding support only.

Site monitoring: barriers and facilitators to recruitment

The main challenge to the trial concerned equipoise, which was a barrier to recruitment both due to staff attitudes and parents' expectations. More than half of women recruited to the trial believed that frenotomy would help their baby and fewer than half were truly in equipoise.

In several areas the onset of the COVID-19 pandemic saw the withdrawal of breastfeeding support services, either in person or at all. In areas where all support was withdrawn, as Trusts did not consider breastfeeding support to be an essential service, the trial had to stop. Similarly in some areas frenotomy lists ceased.

Conclusions

The statistical power of the analysis was extremely limited due to not achieving the target sample size because of the early cessation of the trial and the high proportion of infants in the breastfeeding support arm who underwent frenotomy. There was no evidence of differences between trial arms in any outcomes. Rates of continued breastmilk feeding were high at 3 months in both the frenotomy with breastfeeding support and breastfeeding support groups. Complications of the procedure were not uncommon, occurring in around 1 in 50 infants.

Most infants in the control groups of the five previous trials identified in a previous Cochrane review also underwent frenotomy (77–100%). On this basis all five trials were considered of low quality and at high risk of bias. The 73% frenotomy rate in the breastfeeding support arm that we observed in FROSTTIE is comparable, but on this basis it must also be regarded as at high risk of bias.

This trial does not therefore provide sufficient information to assess whether frenotomy in addition to breastfeeding support improves breastfeeding rates in infants diagnosed with tongue-tie. The effectiveness and cost-effectiveness of the procedure still need to be established. Other study designs will need to be considered to address this objective.

Funding

This project was funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment Programme (project number 16/143/01) and will be published in full in *Health Technology Assessment*; Vol. 27, No. 11. See the NIHR Journals Library website for further project information. The funder had no role in study design or data collection, analysis and interpretation. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

Trial registration

This trial is registered as ISRCTN 10268851.

Chapter 1 Introduction

The World Health Organisation recommends exclusive breastfeeding for at least 6 months because of its many health benefits. Breastmilk-fed infants are less likely to have a range of childhood infections, and protection from infection is greater with longer duration of breastfeeding.[1] Increasing breastfeeding rates is likely to have significant economic benefits based on protection from these infections alone.[2] Similarly, breastfeeding is associated with lower rates of childhood overweight and obesity, and hence a lower likelihood of diabetes as an adult.[3] Breastfeeding and breastfeeding duration is associated with better educational attainment.[4] Mothers who have breastfed have lower rates of both breast and ovarian cancer.[3] Significant sociodemographic inequalities in breastfeeding rates persist,[5] and the latest figures suggest that only around half of babies are still receiving breastmilk at 6 months of age.[6] Interventions to support breastfeeding and breastfeeding duration are therefore important. Breastfeeding support interventions have been shown to be associated with continuation of breastfeeding beyond 10 days.[7]

Breastfeeding difficulties have been associated with many factors, from a societal to an individual level.[8] Tongue-tie can be diagnosed in 3–11% of babies,[9] with the variation in reported prevalence thought to relate to the use of different diagnostic or severity criteria.[10] Up to half of babies with tongue-tie are reported to have breastfeeding difficulties, but the reported proportion is highly variable. Some studies report almost universal difficulties, and others report very few feeding difficulties that relate to the tongue-tie itself, instead noting that incorrect positioning and attachment are the primary reasons behind the observed breastfeeding difficulties and not the tongue-tie itself.[9] In a UK survey,[10] it was noted that management of tongue-tie in infants with breastfeeding difficulties was therefore highly variable across the country. This is coupled with highly variable provision of breastfeeding support,[11] which can range from minimal to expert and intensive, and using a variety of different models including peer supporter, midwife and health visitor.

A Cochrane review[12] identified five prior randomised controlled trials (RCTs) of frenotomy including a total of only 302 infants. The trials are small and underpowered and/or include only very short-term or subjective outcomes, suggesting further robust evidence is needed. Hence there is considerable controversy regarding, not only the diagnosis and clinical significance, but also the management of tongue-tie. Current National Institute for Health and Care Excellence (NICE) guidance[13] allows for the procedure, based on lack of safety concerns, but notes very limited evidence of efficacy. In preparation for this study, we searched the literature to identify previous economic evaluations assessing the cost-effectiveness of frenotomy in a UK setting but no relevant studies were identified. There is therefore a clear need for an assessment of the clinical and cost-effectiveness of frenotomy for babies diagnosed with tongue-tie in the form of an adequately powered, pragmatic RCT, taking into account the diagnostic controversy and variation in practice.

Objective

The objective of this research was to investigate whether frenotomy is clinically and cost-effective to promote continuation of breastfeeding at 3 months in infants with breastfeeding difficulties diagnosed with tongue-tie.

Chapter 2 Methods

Design

The FROSTTIE trial was a multicentre, randomised, controlled parallel group trial conducted in England.

The trial was registered with the International Standard Randomised Controlled Trial Register (ISRCTN 10268851).

Patient and public involvement

The research question was initially prioritised by the NIHR Health Technology Assessment programme, including patient and public involvement (PPI). In order to obtain the perspective of a wide group of women with recent breastfeeding experience and/or experience of tongue-tie, we included a PPI co-applicant from the Breastfeeding Network, who consulted with other Network members, and also established a Public Advisory Group. These two groups helped design the study processes and materials, and advised throughout the trial.

Participants

Inclusion criteria

- Any infant aged <10 weeks referred (by parent or other breastfeeding support service) to an infant feeding service with breastfeeding difficulties and judged to have tongue-tie, whose parent had given informed consent for participation.

Exclusion criteria

Infants were not eligible to enter the study if ANY of the following applied:

- Infant was older than 10 weeks.
- Infant had breastfeeding difficulties but was not judged to have tongue-tie.
- Infant was born at <34 weeks' gestation.
- Infant had a congenital anomaly known to interfere with breastfeeding, for example cleft palate, Down syndrome.
- Infant had a known bleeding diathesis.
- Infant had a frenotomy prior to recruitment.

Setting

The trial was conducted in 12 infant feeding services in England (see *Appendix 1*).

Informed consent and recruitment

Information about the trial was made widely available throughout the infant feeding units in the form of posters and leaflets (with QR codes to the trial website). Written information about the trial was

available to all women at participating centres when they attended for breastfeeding support. In some sites, materials were also available on the postnatal ward.

Potential participants were identified by the infant feeding service staff from the population of infants with breastfeeding difficulties referred to NHS infant feeding services through volunteer breastfeeding supporters, other breastfeeding counsellors, midwives or through self-referral by parents.

As standard, following referral to the infant feeding service, infant feeding was observed (either in person or via video conferencing) and tongue assessment conducted, and mothers received advice on positioning and attachment. Initial discussions may have taken place in person or virtually via telephone or video conferencing if this was what was being offered as part of routine care. The tongue-tie diagnosis was made according to usual hospital practice, which may have included using any suitable tool. However, all babies whose parents consented for their participation in the trial had an assessment of their tongue-tie made using the Bristol Tongue Assessment Tool (BTAT).[14]

Following diagnosis of a tongue-tie associated with breastfeeding difficulties, a verbal explanation and written information (the Parent Information Leaflet) was provided to the parent(s) either as a hardcopy in person or via post, electronically via email or by being directed to the study website. The parent(s) were allowed as much time as they needed to consider the information, and the opportunity to question staff before deciding whether they consented for their baby to participate in the study. Written or remote verbal informed consent was obtained.

Written or verbal informed consent also included optional consent for linkage of their baby's data to routine data sources to allow the potential for further follow-up beyond the funded trial.

Intervention

Infants were randomised via a web randomisation portal to either:

- frenotomy with standard breastfeeding support (intervention arm), or
- no frenotomy with standard breastfeeding support (comparator arm).

Breastfeeding support included as a minimum: an initial assessment of breastfeeding, for example using the LATCH (Latch, Audible swallowing, Type of nipple, Comfort, Hold) tool[15] or Baby Friendly Initiative assessment tool, and advice on positioning and attachment and at least one follow-up visit, together with drop-in clinic advice as required, but available on more than 1 day a week. Assessments and breastfeeding support were provided face-to-face in person or virtually using video conferencing or telephone dependent on what was being offered as part of routine care.

Intervention arm: infants who were randomised to frenotomy with breastfeeding support underwent frenotomy according to usual hospital practice. Frenotomy was carried out by the usual trained practitioner for participating hospitals using their normal technique. The babies had an immediate postfrenotomy observed feed. Parents received further advice on positioning and attachment together with standard postfrenotomy advice concerning bleeding and other postfrenotomy adverse events. Parents were provided with details about how to access rapid breastfeeding support in the event of ongoing feeding difficulties and an appointment for at least one follow-up visit.

Comparator arm: infants randomised to breastfeeding support only did not undergo frenotomy, but received further advice on positioning and attachment. Parents were provided with details about how to

access rapid breastfeeding support in the event of ongoing feeding difficulties and an appointment for at least one follow-up visit.

Randomisation and blinding

The infants entered into the trial were randomised 1 : 1 to either intervention or comparator arm. Multiples (twins or higher-order multiples) were randomised to the same arm. Stratified block randomisation (using variable block sizes) was performed via a secure 24-hour web-based randomisation system [hosted by the National Perinatal Epidemiology Unit (NPEU) Clinical Trials Unit (CTU), University of Oxford] stratified by infant's age (<2 and ≥2 weeks) at randomisation and mother's parity (primiparous or multiparous) within the centre. A telephone back-up system was available 24 hours a day (365 days per year).

A statistician independent of the trial generated the stratified block randomisation (using variable block sizes) schedule and the Senior Trials Programmer wrote the web-based randomisation program; both were independently validated. The implementation of the randomisation procedure was monitored by the Senior Trials Programmer and independent statistician throughout the trial and reports provided to the Data Monitoring Committee (DMC).

Parents were blinded to the allocation for the first 20 participants, following which the trial was conducted unblinded. Blinding consisted of parents being asked not to directly observe the procedure (tongue-tie examination with or without frenotomy) immediately before a postprocedure breastfeed. The request for a change to an unblinded design was made by the funder as it was felt to be a barrier to recruitment.

Internal pilot

We conducted an internal pilot during the first 6 months of the trial, when 266 recruits were predicted, to test recruitment and retention assumptions. The pre-defined stop–go criteria were as follows:

- recruitment 75% or more ($N \geq 199$) – continue directly with the main trial
- recruitment 50–75% ($133 \leq N < 199$) – recruit more centres and review in 6 months
- recruitment < 50% ($N < 133$) – undertake an urgent detailed review of options with Trial Steering Committee (TSC) to subsequently recommend to the funder.

The pilot was restarted in September 2019, following removal of blinding, but was never completed due to a pause in recruitment between March and May 2020 because of the COVID-19 pandemic, and subsequent closure of the trial by the funder.

Outcomes

Primary outcome

Any breastmilk feeding in the 24 hours prior to the infant reaching 3 months of age.[16,17] A positive response was considered indicative of continuation of breastfeeding.

Secondary outcomes

The secondary outcomes were assessed at 3 months of age and some additionally at first follow-up visit (indicated by *).

*Mother's breastfeeding self-efficacy**: measured using the Breastfeeding Self-Efficacy Scale – Short Form

Mother's pain while feeding during the previous 24 hours: measured using visual analogue scale of the Short Form McGill Pain Questionnaire (SF-MPQ), modified into a Likert-type scale

Amount of breastfeeding support used: measured by total number of contacts (whether face-to-face or virtual) with any breastfeeding supporter since the FROSTTIE procedure

Infant weight gain: measured as difference in weight for age *z*-scores between birth and 3 months of age

Infant postrandomisation weight gain: measured as difference in weight for age *z*-scores between baseline and 3 months of age

Exclusive breastmilk feeding:* exclusive breastmilk feeding in the previous 24 hours

Exclusive direct breastfeeding:* exclusive breastfeeding directly from the breast with no bottle feeds of expressed milk in the previous 24 hours

Age of child when s/he last received breastmilk: age when child last received breastmilk, to determine when and whether switch to exclusive formula feeding has occurred

Time spent breastfeeding in previous 24 hours: time in minutes/hours spent breastfeeding in previous 24 hours

Frenotomy in comparator group/repeat frenotomy*/bleeding following frenotomy or frenulum tear*/ post-procedure adverse events (tongue cut*, salivary duct damage*)/maternal and infant NHS health-care resource use):* measured by specific questions

Maternal anxiety and depression: dimension of EuroQol-5 Dimensions, five-level version*

Maternal health-related quality of life: as elicited by the EQ-5D-5L*

Any breastmilk feeding at 6 months: according to maternal self-report: defined as any breastmilk feeding in the 24 hours prior to the infant reaching 6 months of age.

Process outcomes

The process outcomes for all infants included BTAT score by adherence status, reasons for non-adherence, type of breastfeeding support. For infants who had undergone frenotomy additional process outcomes were assessed – role of person performing the procedure, whether anaesthetic was used, whether frenotomy was performed using bipolar diathermy, scissors, or other, frenotomy technique, and whether the infant was able to breastfeed after the procedure.

Sample size

It was assumed that a 10% absolute increase in the rate of breastfeeding represented the minimal clinically important difference that should be detectable by the trial; and breastfeeding rates will remain high in this motivated population. Thus, assuming a breastfeeding rate of 70% in the control group and 80% in the intervention group, at 90% power with a 5% level of significance, and allowing for 5% loss to follow-up, with a further 5% increase to account for between-group contamination required a sample size of 870. Given the final sample size achieved with complete primary outcome data (n = 163), the study had 31% power to detect this difference, assuming the same control group rate.

Statistical analyses

Statistical analyses were carried out according to a pre-specified Statistical Analysis Plan finalised prior to unblinding. For the primary analysis for all primary and secondary outcomes infants, we compared the outcomes of all infants allocated to frenotomy with breastfeeding support with all those allocated to breastfeeding support, regardless of deviation from the protocol or treatment received (referred to as the ITT population). Demographic and clinical data were summarised with counts and percentages for categorical variables, means [standard deviations (SDs)] and medians [with interquartile range (IQR) or simple range] for continuous variables. For binary outcomes, risk ratios (RRs) and confidence intervals (CIs) were calculated using log binomial regression or Poisson regression with a robust variance estimator. Continuous outcomes were analysed using linear or median (quantile) regression for normally distributed and skewed variables, respectively. Analyses were adjusted for stratification factors at randomisation where possible (centre, infant's age at randomisation and mother's parity).[18] Both unadjusted and adjusted risk ratios (aRRs) are presented, with the primary inference based on the adjusted estimates. Two-sided statistical testing was performed throughout. A 5% level of statistical significance was used, and 95% CIs are presented.

Secondary analyses

Four planned secondary analyses were carried out:

1. A comparison of the characteristics and primary outcome by adherence status in the breastfeeding support arm.
2. An assessment of the impact of non-adherence to the randomised allocation using complier-average causal effect (CACE) analysis. The CACE analysis assumes that the proportion of would-be non-compliers in the frenotomy with breastfeeding support arm (i.e. women in this group who would not have complied had they been randomised to breastfeeding support alone) is the same as the proportion of non-compliers in the breastfeeding support arm. It also assumes that the event rate among the non-compliers in the breastfeeding support arm is the same as the event rate among the would-be non-compliers in the frenotomy with breastfeeding support arm. Applying these two assumptions, the event rate for the primary outcome was calculated for the would-be compliers and would-be non-compliers in the frenotomy with breastfeeding support arm. The unadjusted CACE RR and 95% CI for the primary outcome was calculated using the event rates for compliant groups only (i.e. the observed compliers in the breastfeeding support arm and the would-be compliers in the frenotomy arm). The CI for the CACE estimated RR was estimated using the bootstrapping method.
3. Exploratory analysis: a restricted per protocol analysis, excluding participants in the frenotomy with breastfeeding support arm who had no frenotomy performed and participants in the breastfeeding support group who had a frenotomy performed.
4. Exploratory analysis: an as-treated analysis, grouping participants according to the allocation they received (participants in the breastfeeding only group who had a frenotomy performed and received breastfeeding support included in the frenotomy with breastfeeding support arm and participants in the frenotomy with breastfeeding support arm who had no frenotomy performed but received breastfeeding support included in the breastfeeding support group).

Pre-specified subgroup analyses

Four planned subgroup analyses were carried out, examining the primary outcome in the following groups:

- infants aged <2 weeks versus ≥2 weeks at randomisation
- infants with BTAT score 4 or less versus 5–6 versus 7 or more at randomisation
- prior belief concerning frenotomy: likely to be beneficial versus uncertain versus unlikely
- recruited pre- or posttrial pause during the COVID-19 pandemic.

The primary outcome is presented within these subgroups using descriptive statistics only due to the small achieved sample size.

Data collection

Baseline information was collected on sociodemographic and other characteristics at trial entry, including the following:

- infant birthweight
- infant current weight
- estimated date of delivery
- current feeding practices (e.g. expressed breastfeeding, use of infant formula)
- assessment of the degree of tongue-tie using the BTAT
- mother's prior beliefs about frenotomy: using a 3-point Likert scale, the opinions of mothers of infants recruited to the trial were measured at the time of recruitment on their prior belief of the potential benefit of frenotomy
- EQ-5D-5L
- mother's pain while feeding during the previous 24 hours: measured using visual analogue scale of the SF-MPQ, modified into a Likert-type scale (scores ranging from 0 to 10)[16]
- exclusive breastmilk feeding: exclusive breastmilk feeding in the previous 24 hours
- exclusive direct breastfeeding: exclusive breastfeeding directly from the breast with no bottle feeds of expressed milk in the previous 24 hours
- pre-trial entry breastfeeding support received.

The following data were collected from the clinician performing the frenotomy on the day of the procedure:

- in-person BTAT assessment if the baseline assessment was done virtually that is not face-to-face
- intervention undertaken according to randomisation schedule and technique used
- bleeding following frenotomy or frenulum tear
- postprocedure adverse events (tongue cut, salivary duct damage).

The following data were collected from the mother at the routine follow-up visit (approximately 1 to 2 weeks posttrial entry):

- mother's pain while feeding during the previous 24 hours: measured using visual analogue scale of the SF-MPQ, modified into a Likert-type scale (scores ranging from 0 to 10)[16]
- exclusive breastmilk feeding in the previous 24 hours
- exclusive breastfeeding directly from the breast with no bottle feeds of expressed milk in the previous 24 hours
- type of breastfeeding support received (in person or virtual)
- frenotomy/repeat frenotomy (defined as any further procedure on tongue-tie)
- bleeding following frenotomy or frenulum tear
- postprocedure adverse events (tongue cut, salivary duct damage): measured by specific questions
- maternal anxiety or depression as indicated by the anxiety and depression dimension of EQ-5D-5L
- maternal health-related quality of life (HRQoL): as elicited by the EQ-5D-5L.

Data on the primary outcome (any breastmilk feeding in the previous 24 hours at age 3 months) were collected from mothers by automated text message. The following data were collected using maternal self-report via a follow-up link (by smart phone, tablet, computer, postal questionnaire or telephone) when the infant was 3 months of age:

- mother's breastfeeding self-efficacy: measured using the Breastfeeding Self-Efficacy Scale – Short Form[19]
- mother's pain while feeding during the previous 24 hours: measured using visual analogue scale of the SF-MPQ, modified into a Likert-type scale (scores ranging from 0 to 10)[16]
- total number of contacts with any breastfeeding supporter since first referral and specific means of support used (in person or virtual)
- infant weight
- exclusive breastmilk feeding in the previous 24 hours
- exclusive breastfeeding directly from the breast with no bottle feeds of expressed milk in the previous 24 hours
- age when child last received breastmilk, to determine when and whether switch to exclusive formula feeding had occurred[20]
- time spent breastfeeding in previous 24 hours: time in minutes/hours
- frenotomy/repeat frenotomy
- bleeding following frenotomy or frenulum tear
- postprocedure adverse events (tongue cut, salivary duct damage): measured by specific questions
- mother or infant previously diagnosed with COVID-19
- maternal anxiety or depression as indicated by the anxiety and depression dimension of EQ-5D-5L
- maternal HRQoL: as elicited by the EQ-5D-5L
- maternal and infant NHS health-care resource use: collected on general practice visits and hospital admissions.

Data on any breastmilk feeding at 6 months were collected from mothers by automated text message.

Adverse event reporting

Non-serious adverse events were not routinely recorded as the procedure is part of standard clinical practice. However adverse events that were part of the study outcomes [bleeding following frenotomy (unless excessive) or frenulum tear and postprocedure adverse events (tongue cut, salivary duct damage)] were collected as part of standard follow-up.

All serious adverse events (SAEs) were reported immediately, at least within 24 hours; except the following SAEs, which were foreseeable SAEs and were subject to SAE reporting procedures:

- admission or extension of hospital stay due to the following:
    - breastfeeding difficulties
    - poor milk supply in the mother
    - weight loss or poor weight gain in the baby
    - jaundice.

Economic evaluation

A within-trial cost-consequences analysis (CCA) with a time horizon of a 3-month follow-up was conducted from a NHS perspective as the primary analysis for the economic evaluation. In this case, results were presented as benefits and health-care costs in disaggregated format for both mothers and their infants in each treatment arm.[21] Costs included frenotomy and breastfeeding support-related costs, primary care, community care, secondary care and non-NHS related costs. The benefits considered in the CCA were the primary outcome of any breastmilk feeding at 3 months according to maternal self-report, maternal anxiety and depression measured using the relevant EQ-5D-5L domain[22] and HRQoL measured using the EQ-5D-5L at different time points.

In a secondary analysis, a within-trial cost-utility analysis (CUA) from the mother's perspective with a time horizon up to 3 months was also conducted. Quality-adjusted life-years (QALYs), were used to measure benefits in the CUA with mean difference in costs and QALYs were synthesised using the incremental cost-effectiveness ratio (ICER) expressed as incremental costs per QALYs gained over the trial period.[23] The ICER was compared to the standard cost-effectiveness threshold as recommended by NICE to determine value for money.[24]

NHS health-care resource use

Detailed information on health-care resource use was collected for women and their infants and included data on resource utilisation up to 3 months after birth. Frenotomy-related resource use was collected directly from the health-care professional undertaking the procedure. Infant and maternal health-care resource use was collected using questionnaires at the routine follow-up visit (approximately 1 to 2 weeks posttrial entry) and when the infant was three months of age. The latter one could be completed by smart phone, tablet, computer, postal questionnaire or telephone.

Health-care utilisation related to frenotomy intervention

Frenotomy-related resource use data were collected from the health-care professional performing the procedure on the day of the operation and included who performed the procedure and whether any complications occurred. The setting where the frenotomy was conducted (NHS setting or private provided) was facilitated by mothers at her routine follow-up visit or using the 3-month follow-up questionnaire.

Health-care utilisation related to breastfeeding support

Resource use data on breastfeeding support were collected using the maternal questionnaire when the infant was 3 months of age. Resource use data in this category included type of breastfeeding support service, whether it was delivered face-to-face or remotely and how many times the service was used. We also collected information on any out of pocket expenses incurred due to visits to any breastfeeding support service consultations.

Primary, community and secondary health-care utilisation

Primary and community health-care utilisation for both mothers and their infants were collected using the maternal questionnaire when the infant was 3 months of age. Primary care visits included general practitioner and practice nurse visits, medication prescribed to treat anxiety or depression, and antibiotic use (reason and number of courses received). Community care contacts included visits to community nurse or midwife contacts, infant health visitor contacts and community paediatrician visits. Secondary (hospital-based) care contacts included accident and emergency department visits, hospital outpatient clinic appointments and hospital overnight admissions. We also collected any other NHS contact to a health-care professional not captured by the previous categories and visits to non-NHS health-care professionals up to 3 months follow-up. The different items of resource use collected for each category are presented in *Appendix 2*, *Table 22*.

Unit cost data collection

Sources and associated estimates of unit costs for the different resource use categories are presented in *Appendix 2*, *Table 22*. Unit costs were extracted from national sources, including NHS Reference Costs 2019/2020 Version 2,[25] Unit costs of Health and Social Care 2020[26] and the Electronic Drug Tariff March 2020.[27] Given the reason for the antibiotics prescribed, the generic name of the antibiotic for the medicine costs analysis was assumed based on the national guidelines.[28,29] Prescription cost analysis 2020/21 data were then used to determine the antibiotic's most prescribed form and dosage.[30] Hospital admissions were costed using the weighted average of a non-elective short stay across relevant Health-care Resource Group codes for the reason for

admission from the NHS Reference Costs. We assumed that breastfeeding services received outside a NHS setting did not incur any costs unless reported specifically by the mother as out of pocket expenses. The only other non-NHS health-care professional visits reported was a contact with an osteopath, which was costed individually from the best source available to the research team.[31] All costs were expressed in 2019/20 pounds sterling.

Health outcome measures

In the CCA, health outcome measures included the primary clinical effectiveness of any breastmilk feeding at 3 months according to maternal self-report as described above, maternal anxiety and depression as measured by the relevant EQ-5D-5L dimension, and HRQoL at different follow-up periods as measured by EQ-5D-5L index values.

The EQ-5D-5L is a multiattribute generic instrument for measuring HRQoL. EQ-5D-5L consists of a descriptive system to describe health state and a visual analogue scale to evaluate overall level of health.[22] In this study, only results from the descriptive system are reported. The instrument covers five dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression, and each dimension has associated five-levels ranging from no problems to unable/extreme problems. The EQ-5D-5L describes 3125 health state profiles that need to be converted into a single preference-based score (HRQoL) using a value set obtained from a representative sample of the general population to be used in economic evaluations.[22]

At the time of conducting this economic evaluation, the recommended approach to estimate EQ-5D-5L preference-based scores (HRQoL) was to convert EQ-5D-5L responses onto EQ-5D-3L preference-based scores using a mapping algorithm.[32] This mapping was based on the recent exercise conducted by Hernández-Alava and colleagues to derive EQ-5D-3L utility values from the existing EQ-5D-5L data.[33] The EQ-5D-5L questionnaire was completed by mother at the trial entry, at the routine follow-up visit (approximately 1 to 2 weeks posttrial entry) and when the infant was 3 months of age.

In the CUA, the main measure of benefits was maternal QALYs [also expressed as quality-adjusted life-days (QALDs) to facilitate interpretation given short time horizon]. Maternal QALDs and QALYs were derived as the area under the curve for the health profile created connecting EQ-5D-5L values at trial entry, at the routine follow-up visit, and 3 months after birth. A straight line relationship was assumed between the maternal utility values at the different time points.

Statistical analysis

We summarised the information about frenotomy procedures in each group using frequencies and associated proportions. Mean and SD were used to present the different categories of NHS health-care resource use and costs in each trial arm. Resource use is presented across all participants in the study and only for those who consumed a particular health-care resource use category. A mean difference between trial arms adjusted for the centre, infant's age at randomisation and parity with associated 95% CI was computed using a generalised linear model. We present resource use and costs separately for mothers and their infants, but main categories of costs [primary care, medicines, community care, secondary (hospital-based) care, other NHS health-care professionals' contacts, other non-NHS health care] were also presented as a single value combining information from both. Mean (SD) for each group with associated adjusted mean difference using the same approach as for costs was calculated to present EQ-5D-5L scores at baseline (trial entry), routine follow-up (approximately 1 to 2 weeks posttrial entry), 3 months after birth and overall QALYs or QALDs. The distribution of responses across the EQ-5D-5L dimensions was presented as frequencies and proportions at baseline (trial entry), routine follow-up (approximately 1 to 2 weeks posttrial entry) and 3 months after birth. Pearson's chi-squared test was used to examine differences in the distribution of EQ-5D-5L responses between the two groups.

For all categories of NHS resource use, costs, HRQoL and QALYs we report the number of participants with missing data. The summary of the cost-consequence analysis therefore used different sample sizes for each of the components presented. However, the within-trial CUA was presented using a complete case analysis where mothers have complete information on total costs and QALYs over the trial period. The ICER was expressed as the ratio of the mean difference in costs divided by the mean difference in QALYs between the two groups. The breastfeeding support only arm was used as the comparator in the ICER calculation. Uncertainty around the ICER was evaluated using 95% CIs from a non-parametric bootstrap approach using 1000 replicates. Bootstrap replicates of mean difference in costs and effects were presented in the cost-effectiveness plane (CEP). Current thresholds of willingness to pay for QALY gained of £20,000 was used to determine value for money. Cost-effectiveness acceptability curves were derived to evaluate whether frenotomy when compared with breastfeeding support was cost-effective at different thresholds of willingness to pay.

The statistical analysis was conducted in Stata/MP version 17.0 and Microsoft Excel.

Governance and monitoring

A monitoring plan for the trial, including responsibilities, was developed prior to the start of recruitment. In person monitoring of all sites was carried out to identify barriers and facilitators to recruitment and the findings of the visits summarised to guide ongoing actions to enhance recruitment.

The trial was supervised on a day to day basis by a Project Management Group. A TSC was convened including an independent chair, four other independent members, a PPI representative(s), the NPEU CTU Director and the Chief Investigator. A DMC independent of the applicants and of the TSC reviewed the progress of the trial annually and provided advice on the conduct of the trial to the TSC.

Summary of changes to the study protocol

Masking of parents was removed from the trial at the funder request after a short pilot period as it was felt to be a barrier to recruitment. Following the restart after the first wave of the COVID-19 pandemic, changes were made to allow virtual assessments and breastfeeding support, and virtual BTAT assessment. Verbal consent was permitted if written consent was not possible. The COVID-19 status of mother and baby was added to the data collection.

A summary of the other changes made to the original protocol is presented in *Appendix 3*.

Chapter 3 Results

Recruitment and retention

Between March 2019 and November 2020, 169 infants were randomised; 80 to the frenotomy with breastfeeding support arm and 89 to the breastfeeding support arm. There were no substantial differences in the response rates between the intervention arms during the follow-up period (see *Figure 1*). The trial was stopped in November 2020 in the context of the COVID-19 pandemic due to withdrawal of breastfeeding support services, slow recruitment and crossover between arms. In the frenotomy with breastfeeding support arm 74/80 infants (93%) received their allocated intervention, compared to 23/89 (26%) in the breastfeeding support arm.

The number of participants recruited at each site varied from 1 to 85 (see *Table 1*).

Characteristics of participants

Characteristics of participants were similar between the two trial arms. Infants had a mean age of 3 weeks, a mean birthweight of 3439 g and 87% were born at ≥38 weeks' gestation. Overall 33% of infants had a BTAT score of 4 or less, 66% had exclusive breastmilk feeding in the previous 24 hours, and 40% had exclusive direct breastmilk feeding. Thirty-four per cent of infants had also received formula milk in the previous 24 hours (see *Table 1*). Mothers were a mean of 32 years old, 94% were of white ethnicity and 48% had a previous live birth. Only 8% were resident in the most deprived quintile of areas. Mothers reported a mean pain score of 4 out of 10 while feeding during the previous 24 hours and 42% had some anxiety or depression. More than half of women recruited to the trial believed a frenotomy would help their baby (see *Table 2*). Only one infant, in the breastfeeding support group, was reported to have had COVID-19.

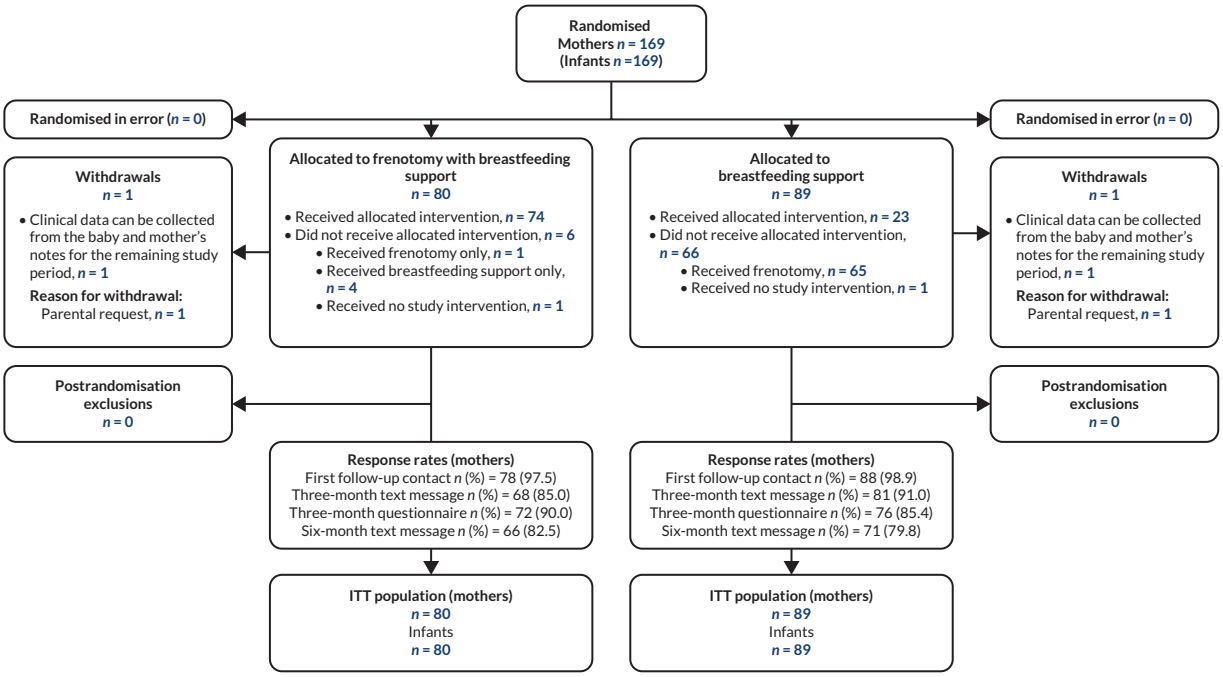

FIGURE 1 Flow of participants.

TABLE 1 Infant characteristics at trial entry

	Total (*n* = 169)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)
Gestational age at birth			
34^{+0} to 35^{+6} weeks, *n* (%)	7 (4.1)	3 (3.8)	4 (4.5)
36^{+0} to 37^{+6} weeks, *n* (%)	15 (8.9)	6 (7.5)	9 (10.1)
38^{+0} to 39^{+6} weeks, *n* (%)	71 (42.0)	35 (43.8)	36 (40.5)
40^{+0} to 42^{+6} weeks, *n* (%)	76 (45.0)	36 (45.0)	40 (44.9)
Age at randomisation[a]			
<2 weeks, *n* (%)	64 (37.9)	30 (37.5)	34 (38.2)
≥2 and <4 weeks, *n* (%)	48 (28.4)	24 (30.0)	24 (27.0)
≥4 and <10 weeks, *n* (%)	57 (33.7)	26 (32.5)	31 (34.8)
≥10 weeks, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
Birthweight (g), mean (SD)	3439.3 (561.3)	3409.0 (563.6)	3466.5 (561.1)
Birthweight *z*-score (adjusted for gestational age and sex at birth),[b] **median (IQR)**	−0.4 (−1.0 to 0.2)	−0.5 (−1.2 to 0.3)	−0.3 (−0.8 to 0.2)
Current weight (g, within last 7 days), mean (SD)	3832.2 (857.7)	3767.8 (841.0)	3890.7 (873.4)
Missing, *n*	3	1	2
Mode of birth			
Unassisted vaginal, *n* (%)	87 (51.5)	42 (52.5)	45 (50.6)
Assisted vaginal, *n* (%)	26 (15.4)	14 (17.5)	12 (13.5)
Vaginal breech, *n* (%)	1 (0.6)	1 (1.3)	0 (0.0)
C-section before labour onset, *n* (%)	22 (13.0)	7 (8.8)	15 (16.9)
C-section after labour onset, *n* (%)	33 (19.5)	16 (20.0)	17 (19.1)
Sex			
Male, *n* (%)	100 (59.2)	51 (63.8)	49 (55.1)
Female, *n* (%)	69 (40.8)	29 (36.2)	40 (44.9)
Missing, *n* (%)	0	0	0
Degree of tongue-tie (BTAT)			
0–4, *n* (%)	55 (32.7)	29 (36.3)	26 (29.6)
5–6, *n* (%)	53 (31.6)	21 (26.3)	32 (36.4)
7–8, *n* (%)	60 (35.7)	30 (37.5)	30 (34.1)
Missing, *n*	1	0	1
Exclusive breastmilk feeding in the previous 24 hours[c]			
Yes, *n* (%)	111 (65.7)	51 (63.8)	60 (67.4)
No, *n* (%)	58 (34.3)	29 (36.2)	29 (32.6)

TABLE 1 Infant characteristics at trial entry (*continued*)

	Total (*n* = 169)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)
Exclusive direct breastfeeding in the past 24 hours[d]			
Yes, *n* (%)	67 (39.6)	30 (37.5)	37 (41.6)
No, *n* (%)	102 (60.4)	50 (62.5)	52 (58.4)
Use of infant formula			
Yes, *n* (%)	57 (33.7)	28 (35.0)	29 (32.6)
No, *n* (%)	112 (66.3)	52 (65.0)	60 (67.4)
Phototherapy for jaundice			
Yes, *n* (%)	23 (13.6)	10 (12.5)	13 (14.6)
No, *n* (%)	146 (86.4)	70 (87.5)	76 (85.4)
NICU admission	19 (11.2)	9 (11.3)	10 (11.2)
1–2 nights, *n* (%)	8 (44.4)	4 (50.0)	4 (40.0)
3–4 nights, *n* (%)	3 (16.7)	2 (25.0)	1 (10.0)
>4 nights, *n* (%)	7 (38.9)	2 (25.0)	5 (50.0)
Missing, *n*	1	1	0
Baby is one of a multiple pregnancy			
Yes, *n* (%)	1 (0.6)	1 (1.2)	0 (0.0)
No, *n* (%)	168 (99.4)	79 (98.8)	89 (100.0)
Sibling enrolled in the study (in multiple pregnancies)			
Yes, *n* (%)	0 (0.0)	0 (0.0)	Not applicable
No, *n* (%)	1 (100.0)	1 (100.0)	
Recruiting centre[a]			
Cumberland Infirmary, *n* (%)	1 (0.6)	1 (1.2)	0 (0.0)
George Eliot Hospital, *n* (%)	2 (1.2)	2 (2.5)	0 (0.0)
Norfolk and Norwich University Hospital, *n* (%)	85 (50.3)	39 (48.8)	46 (51.7)
Queen Alexandra Hospital, *n* (%)	1 (0.6)	0 (0.0)	1 (1.1)
Royal Albert Edward Infirmary, *n* (%)	5 (3.0)	2 (2.5)	3 (3.4)
Royal Berkshire Hospital, *n* (%)	24 (14.2)	12 (15.0)	12 (13.5)
Royal Blackburn Hospital, *n* (%)	13 (7.7)	7 (8.8)	6 (6.7)
Royal Cornwall Hospital, *n* (%)	5 (3.0)	2 (2.5)	3 (3.4)
Royal United Hospital, Bath, *n* (%)	1 (0.6)	0 (0.0)	1 (1.1)
Royal Victoria Infirmary, *n* (%)	26 (15.4)	12 (15.0)	14 (15.7)
Stoke Mandeville Hospital, Aylesbury, *n* (%)	1 (0.6)	1 (1.3)	0 (0.0)
Sunderland Royal Hospital, *n* (%)	5 (3.0)	2 (2.5)	3 (3.4)

a Stratification factor.
b Vidar SI, Cole TJ, Pan H. Standardizing anthropometric measures in children and adolescents with functions for egen: update, *Stata J* 2013;**13**(2):366–78.
c Exclusive breastmilk feeding including bottle feeds of expressed milk in the previous 24 hours.
d Exclusive breastfeeding directly from the breast with no bottle feeds of expressed milk in the previous 24 hours.

TABLE 2 Maternal characteristics at trial entry

	Total *n* = 169)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)
Mother's age (years), mean (SD)	32.3 (5.0)	32.7 (4.8)	31.9 (5.1)
Missing, *n*	6	3	3
Mother's ethnic group			
White, *n* (%)	156 (94.0)	72 (92.3)	84 (95.5)
Asian, *n* (%)	7 (4.2)	5 (6.4)	2 (2.3)
Black, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
Mixed, *n* (%)	3 (1.8)	1 (1.3)	2 (2.3)
Other, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
Missing, *n*	3	2	1
Index of multiple deprivation of area of residence			
1 (most deprived), *n* (%)	13 (7.7)	3 (3.8)	10 (11.2)
2, *n* (%)	40 (23.7)	22 (27.5)	18 (20.2)
3, *n* (%)	38 (22.5)	21 (26.3)	17 (19.1)
4, *n* (%)	40 (23.7)	15 (18.8)	25 (28.1)
5 (least deprived), *n* (%)	38 (22.5)	19 (23.8)	19 (21.4)
Previous live birth(s)[a]			
Yes, *n* (%)	81 (47.9)	39 (48.7)	42 (47.2)
No, *n* (%)	88 (52.1)	41 (51.3)	47 (52.8)
Breastfed before			
Yes, *n* (%)	73 (92.4)	33 (89.2)	40 (95.2)
No, *n* (%)	6 (7.6)	4 (10.8)	2 (4.8)
Not applicable – no previous live birth, *n*	88	41	47
Missing, *n*	2	2	0
Pre-trial breastfeeding support received			
Yes, *n* (%)	140 (84.3)	66 (84.6)	74 (84.1)
No, *n* (%)	26 (15.7)	12 (15.4)	14 (15.9)
Missing, *n*	3	2	1
Mother's pain while feeding during previous 24 hours,[b] **median (IQR)**	4 (2–7)	4 (1–7)	4 (2–7)
Missing, *n*	3	2	1
Mother's prior beliefs about frenotomy			
Think it will help my baby, *n* (%)	86 (51.8)	41 (52.6)	45 (51.1)
Do not know if it will help my baby, *n* (%)	79 (47.6)	37 (47.4)	42 (47.7)
Think it is unlikely to help my baby, *n* (%)	1 (0.6)	0 (0.0)	1 (1.1)
Missing, *n*	3	2	1

TABLE 2 Maternal characteristics at trial entry (*continued*)

	Total *n* = 169)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)
Maternal anxiety or depression[c]			
Yes, *n* (%)	69 (41.8)	29 (37.2)	40 (46.0)
No, *n* (%)	96 (58.2)	49 (62.8)	47 (54.0)
Missing, *n*	4	2	2
Maternal HRQoL,[d] **mean (SD)**	0.77 (0.17)	0.77 (0.18)	0.77 (0.16)
Missing, *n*	8	4	4
Recruited pre- or posttrial pause[e] **during the COVID-19 pandemic**			
Pre-pause, *n* (%)	107 (63.3)	52 (65.0)	55 (61.8)
Postpause, *n* (%)	62 (36.7)	28 (35.0)	34 (38.2)

a Stratification factor.
b Measured using visual analogue scale of the SF-MPQ, modified into a 10-point Likert scale.
c Anxiety and depression dimension of EQ-5D-5L categorised into levels 2–5 (presence of anxiety/depression) and level 1 (no anxiety/depression).
d EQ-5D-5L overall index value.
e Trial paused recruitment on 17 March 2020 and resumed on 22 May 2020.

Outcomes

Primary outcomes

Primary outcome data were available for 163/169 infants (96%). There was no evidence of a difference between the arms in the rate of breastmilk feeding at 3 months, which was high in both groups (67/76, 88% vs. 75/87, 86%; aRR 1.02, 95% CI 0.90 to 1.16) (see *Table 3*).

Secondary outcomes

There was no evidence of differences between the intervention arms for any secondary outcomes (see *Tables 4* and *5*). Sixty-three infants in the breastfeeding support only arm had undergone frenotomy by their first follow-up visit. An additional two infants underwent frenotomy by the third month of follow-up. None of the infants had a repeat frenotomy. Adverse events were reported for three infants postsurgery (one infant had bleeding, one infant had salivary duct damage, and the third infant had accidental cut to the tongue and salivary duct damage) (see *Tables 4–6*). No other causally related SAEs were reported.

TABLE 3 Primary outcome at 3 months of age

	Total (*n* = 169)	Frenotomy w/ breastfeeding Support (*n* = 80)	Breastfeeding support (*n* = 89)	Unadjusted risk ratio (95% CI)	Adjusted risk ratio (95% CI)	*p*-value
Any breastmilk feeding[b]						
Yes, *n* (%)	142 (87.1)	67 (88.2)	75 (86.2)	1.02 (0.91 to 1.15)	1.02 (0.90 to 1.16)	0.73
No, *n* (%)	21 (12.9)	9 (11.8)	12 (13.8)			
Missing, *n*	6	4	2			

a Adjusted for centre, infant's age at randomisation, and parity.
b According to maternal self-report, defined as any breastmilk feeding in the 24 hours prior to the infant reaching 3 months of age.

TABLE 4 Secondary outcomes at first follow-up visit (1–2 weeks postrandomisation)

	Total (*n* = 169)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)	Unadjusted effect estimate (95% CI)	Adjusted[a] effect estimate (95% CI)	*p*-value
Exclusive breastmilk feeding in the previous 24 hours[b]						
Yes, *n* (%)	117(70.9)	51 (65.4)	66 (75.9)	0.86 (0.60 to 1.24)	0.86 (0.59 to 1.24)	0.42
No, *n* (%)	48 (29.1)	27 (34.6)	21 (24.1)			
Missing, *n*	4	2	2			
Exclusive direct breastfeeding in the past 24 hours[c]						
Yes, *n* (%)	78 (47.3)	35 (44.9)	43 (49.4)	0.91 (0.58 to 1.42)	0.92 (0.59 to 1.45)	0.73
No, *n* (%)	87 (52.7)	43 (55.1)	44 (50.6)			
Missing, *n*	4	2	2			
Mother's pain while feeding during previous 24 hours,[d] **median (IQR)**	2 (0–4)	2 (0–4)	2 (0–4)	0.0 (−0.9 to 0.9)	0.0 (−0.9 to 0.9)	0.99
Not currently breastfeeding, *n*	3	2	1			
Missing, *n*	4	2	2			
Maternal anxiety or depression[e]						
Yes, *n* (%)	52 (31.7)	23 (29.9)	29 (33.3)	0.90 (0.52 to 1.55)	0.92 (0.53 to 1.63)	0.79
No, *n* (%)	112 (68.3)	54 (70.1)	58 (66.7)			
Missing, n	5	3	2			
Frenotomy performed				-	-	-
Yes, *n* (%)	138 (81.7)	75 (93.8)	63 (70.8)	-	-	-
No, *n* (%)	31 (18.3)	5 (6.2)	26 (29.2)	-	-	-
Missing, *n*	0	0	0	-	-	-

a Adjusted for centre, infant's age at randomisation and parity.
b Exclusive breastmilk feeding including bottle feeds of expressed milk in the previous 24 hours.
c Exclusive breastfeeding directly from the breast with no bottle feeds of expressed milk in the previous 24 hours.
d Measured using visual analogue scale of the SF-MPQ, modified into a 10-point Likert scale.
e Anxiety and depression dimension of EQ-5D-5L categorised into levels 2–5 (presence of anxiety/depression) and level 1 (no anxiety/depression).

Note
The effect estimates are risk ratios for all variables except mother's pain while feeding for which the estimate is median difference.

TABLE 5 Secondary outcomes at 3 months of age

	Total (*n* = 169)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)	Unadjusted effect estimate (95% CI)	Adjusted[a] effect estimate (95% CI)	*p*-value
Mother's breastfeeding self-efficacy,[b] median (IQR)	58 (47–65)	60 (47–65)	56.5 (47–65)	4 (−1.8 to 9.8)	0.3 (−5.2 to 5.8)	0.92
(Min to max)	(14, 70)	(14, 70)	(14, 70)			
Missing, *n*	26	11	15			
Exclusive breastmilk feeding in the previous 24 hours[c]						
Yes, *n* (%)	95 (65.1)	45 (63.4)	50 (66.7)	0.95 (0.64 to1.42)	0.92 (0.61 to 1.39)	0.69
No, *n* (%)	51 (34.9)	26 (36.6)	25 (33.3)			
Missing, *n*	23	9	14			
Exclusive direct breastfeeding in the past 24 hours[d]						
Yes, *n* (%)	77 (53.1)	38 (53.5)	39 (52.7)	1.02 (0.65 to 1.59)	1.03 (0.65 to 1.62)	0.90
No, *n* (%)	68 (46.9)	33 (46.5)	35 (47.3)			
Missing, *n*	24	9	15			
Mother's pain while feeding during previous 24 hours,[e] median (IQR)	0 (0–1.5)	0 (0–1)	0 (0–2)	0 (−0.5 to 0.5)	−0.2 (−0.6 to 0.3)	0.45
Missing, *n*	24	10	14			
Not currently breastfeeding, *n*	21	9	12			
Amount of breastfeeding support used (number of contacts),[f] median (IQR)	3 (1–4)	3 (2–5)	2 (1–4)	1 (0.1 to 1.9)	−0.3 (−1.5 to 1.0)	0.68
Missing, *n*	22	8	14			
Not applicable, *n*[g]	36	22	14			
Maternal anxiety or depression[h]						
Yes, *n* (%)	55 (37.2)	29 (39.7)	26 (34.7)	1.15 (0.67 to 1.95)	1.12 (0.65 to 1.93)	0.69

continued

TABLE 5 Secondary outcomes at 3 months of age (*continued*)

	Total (*n* = 169)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)	Unadjusted effect estimate (95% CI)	Adjusted effect estimate (95% CI)	*p*-value
No, *n* (%)	93 (62.8)	44 (60.3)	49 (65.3)			
Missing, *n*	21	7	14			
Maternal HRQoL,[i] median (IQR)	0.9 (0.8–1.0)	0.9 (0.8–1.0)	0.9 (0.8–1.0)	0.0 (−0.1 to 0.1)	0.0 (−0.1 to 0.1)	0.94
Missing, *n*	23	8	15			
Infant weight gain from birth (*z*-score),[j] mean (SD)	−1.2 (1.2)	−1.1 (1.3)	−1.2 (1.1)	0.10 (−0.62 to 0.82)	0.17 (−0.60 to 0.95)	0.65
Infant weight gain from randomisation (*z*-score),[j] mean (SD)	−1.1 (1.4)	−1.0 (1.6)	−1.1 (1.3)	0.04 (−0.82 to 0.90)	0.10 (−0.83 to 1.03)	0.83
Frenotomy performed						
Yes, *n* (%)	140 (82.8)	75 (93.8)	65 (73.0)	-	-	-
No, *n* (%)	29 (17.2)	5 (6.2)	24 (27.0)			
Missing, *n*	0	0	0	-	-	-
Infants who continued to breastfeed	***n* = 142**	***n* = 67**	***n* = 75**			
Time spent breastfeeding in previous 24 hours (hours), median (IQR)	3 (2–5)	3 (2–5)	3 (2–4)	0 (−1.1 to 1.1)	0.1 (−1.1 to 1.2)	0.90

a Adjusted for centre, infant's age at randomisation and parity.
b Assessed by breastfeeding self-efficacy scale – short form.
c Exclusive breastmilk feeding including bottle feeds of expressed milk in the previous 24 hours.
d Exclusive breastfeeding directly from the breast with no bottle feeds of expressed milk in the previous 24 hours.
e Measured using visual analogue scale of the SF-MPQ, modified into a 10-point Likert scale.
f Number of times seen or spoken to a breastfeeding supporter/counsellor as reported on the 3-month questionnaire.
g Answered no to the question about 'seen or spoken to a breastfeeding supporter/counsellor' at the 3-month follow-up.
h Anxiety and depression dimension of EQ-5D-5L categorised into levels 2–5 (presence of anxiety/depression) vs. level 1 (no anxiety/depression).
i EQ-5D-5L overall index value.
j Vidar SI, Cole TJ, Pan H. Standardizing anthropometric measures in children and adolescents with functions for egen: update'. *Stata J* 2013;**13**(2):366–78.

Note
The effect estimates are risk ratios for categorical outcomes, median difference for continuous outcomes except for infant weight gain from birth and randomisation for which the effect estimate is mean difference.

TABLE 6 Time to frenotomy among infants who had frenotomy in the first 3 months after randomisation

	Total (*n* = 140)	Frenotomy w/ breastfeeding support (*n* = 75)	Breastfeeding support (*n* = 65)
Age of infant at first frenotomy (days), median (IQR)	24 (13–38)	23 (11–35)	26.5 (16–42.5)
Missing, *n*	1	0	1
Time from randomisation to frenotomy (days)			
<1 day, *n* (%)	42 (30.2)	30 (40.0)	12 (18.8)
1–2 days, *n* (%)	34 (24.5)	20 (26.7)	14 (21.9)
3–6 days, *n* (%)	22 (15.8)	12 (16.0)	10 (15.6)
7–13 days, *n* (%)	26 (18.7)	10 (13.3)	16 (25.0)
14–<28 days, *n* (%)	10 (7.2)	3 (4.0)	7 (10.9)
≥28 days, *n* (%)	5 (3.6)	0 (0.0)	5 (7.8)
Missing, *n*	1	0	1

Data on age at cessation of breastfeeding was only available for 6/21 infants, five in the breastfeeding support arm, who stopped breastfeeding at a median of 5 weeks (IQR 5–7).

Mothers had high breastfeeding self-efficacy at 3 months' follow-up and exclusive breastfeeding rates were high during follow-up (first follow-up: 71%, third month: 65%). Compared to first follow-up, pain during breastfeeding was lower at 3 months (median score out of 10: 0 vs. 2).

Process outcomes

In the frenotomy with breastfeeding support arm, 74/80 (93%) received the allocated intervention whereas in the breastfeeding support arm this was 23/89 (26%). More than four-fifths of the infants in the breastfeeding support arm who adhered to their allocation (19/23, 83%) had a BTAT score >4. Infants in the breastfeeding support arm who had a frenotomy had the operation a median of 5.5 days after randomisation (IQR 2–9 days). Frenotomies were mostly performed by midwives, the technique most commonly used was division of an anterior membrane plus posterior fleshy attachment, and 85% of infants were able to breastfeed immediately after the procedure (see *Table 7*).

Exploratory analyses

There was no significant difference (aRR 1.27, 95% CI 0.99 to 1.64) in the rate of breastmilk feeding at 3 months between the arms per protocol analysis where the 70 infants who did not receive their allocated intervention were excluded (infants in the frenotomy with breastfeeding support who had no frenotomy performed and infants in the breastfeeding only group who had a frenotomy performed) (see *Table 8*).

There was a significant difference in the rate of breastmilk feeding at 3 months in the as-treated analysis where infants were analysed according to the intervention received (RR 1.35, 95% CI 1.05 to 1.74), noting that for this analysis, the groups compared were not the groups originally randomised and hence this difference may be due to confounders not accounted for in the analysis (see *Table 9*).

TABLE 7 Process outcomes

	Total (*n* = 169)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)
Allocation adhered to[a]			
Yes, *n* (%)	97 (57.4)	74 (92.5)	23 (25.8)
BTAT score 0–4 at randomisation, *n* (%)	31 (32.0)	27 (36.5)	4 (17.4)
BTAT score 5–6 at randomisation, *n* (%)	28 (28.9)	20 (27.0)	8 (34.8)
BTAT score 7–8 at randomisation, *n* (%)	38 (39.2)	27 (36.5)	11 (47.8)
No, *n* (%)	72 (42.6)	6 (7.5)	66 (74.2)
BTAT score 0–4 at randomisation, *n* (%)	24 (33.8)	2 (33.3)	22 (33.9)
BTAT score 5–6 at randomisation, *n* (%)	25 (35.2)	1 (16.7)	24 (36.9)
BTAT score 7–8 at randomisation, *n* (%)	22 (31.0)	3 (50.0)	19 (29.2)
Missing, *n*	1	0	1
Received no intervention, *n* (%)	2 (1.2)	1 (1.3)	1 (1.1)
Reason for non-adherence			
Parental wish, *n* (%)	5 (23.8)	4 (80.0)	1 (6.3)
Clinician decision, *n* (%)	2 (9.5)	1 (20.0)	1 (6.3)
Other,[b] *n* (%)	14 (66.7)	0 (0.0)	14 (87.5)
Missing, *n*	51	1	50
Type of breastfeeding support received			
In person, *n* (%)	29 (26.4)	15 (30.0)	14 (23.3)
Virtual, *n* (%)	45 (40.9)	18 (36.0)	27 (45.0)
In person and virtual, *n* (%)	36 (32.7)	17 (34.0)	19 (31.7)
Missing, *n*	56	28	28
Not applicable,[c] *n*	3	2	1
Infants who underwent frenotomy	**(*n* = 140)**	**(*n* = 75)**	**(*n* = 65)**
Person performing procedure			
Midwife, *n* (%)	117 (85.4)	61 (81.3)	56 (90.3)
Nurse, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
Doctor, *n* (%)	19 (13.9)	13 (17.3)	6 (9.7)
Other, *n* (%)	1 (0.7)	1 (1.3)	0 (0.0)
Missing, *n*	3	0	3
Frenotomy performed with			
Bipolar diathermy, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
Scissors, *n* (%)	129 (100.0)	75 (100.0)	54 (100.0)
Missing, *n*	11	0	11
Technique			
Division of an anterior membrane only, *n* (%)	12 (9.2)	11 (14.7)	1 (1.8)

TABLE 7 Process outcomes (*continued*)

	Total (*n* = 169)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)
Division of an anterior membrane plus posterior fleshy attachment, *n* (%)	102 (78.5)	54 (72.0)	48 (87.3)
Division of posterior fleshy attachment only, *n* (%)	14 (10.8)	8 (10.7)	6 (10.9)
Other, *n* (%)	2 (1.5)	2 (2.7)	0 (0.0)
Missing, *n*	10	0	10
Baby able to breastfeed after procedure			
Straight away, *n* (%)	116 (84.7)	65 (86.7)	51 (82.3)
Within 15 minutes, *n* (%)	11 (8.0)	6 (8.0)	5 (8.1)
No, *n* (%)	10 (7.3)	4 (5.3)	6 (9.7)
Missing, *n*	3	0	3

a Non-adherence: allocated to frenotomy w/breastfeeding support but did not receive either frenotomy, breastfeeding support or both or allocated to breastfeeding support but did receive a frenotomy or did not receive breastfeeding support.
b Specific reasons listed for non-adherence in these 14 infants were as follows: concerns over weight loss/growth (*n* = 1), maternal pain/distress (*n* = 5), continuing feeding difficulties (*n* = 3), concerns over weight loss/growth and maternal pain/distress (*n* = 2), concerns over weight loss/growth and continuing feeding difficulties (*n* = 2), and concerns over weight loss/growth, maternal pain/distress and continuing feeding difficulties (*n* = 1).
c Did not receive breastfeeding support.

TABLE 8 Exploratory analysis: primary outcome (restricted per-protocol analysis)

	Total (*n* = 99)	Frenotomy w/ breastfeeding support (*n* = 75)	Breastfeeding support (*n* = 24)	Unadjusted risk ratio (95% CI)	Adjusted[a] risk ratio (95% CI)	*p*-value
Any breastmilk feeding[b]						
Yes, *n* (%)	81 (86.2)	65 (90.3)	16 (72.7)	1.24 (0.95 to 1.62)	1.27 (0.99 to 1.64)	0.06
No, *n* (%)	13 (13.8)	7 (9.7)	6 (27.3)			
Missing, *n*	5	3	2			

a Adjusted for centre, infant's age at randomisation and parity.
b According to maternal self-report, defined as any breastmilk feeding in the 24 hours prior to the infant reaching 3 months of age.

TABLE 9 Exploratory analysis: primary outcome (as-treated analysis)

	Total (*n* = 166)	Received frenotomy w/ breastfeeding support (*n* = 139)	Received breastfeeding support only (*n* = 27)	Unadjusted risk ratio (95% CI)	Adjusted[a] risk ratio (95% CI)	*p*-value
Any breastmilk feeding[b]						
Yes, *n* (%)	141 (87.0)	123 (90.4)	18 (69.2)	1.31 (1.00 to 1.70)	1.35 (1.05 to 1.74)	0.02
No, *n* (%)	21 (13.0)	13 (9.6)	8 (30.8)			
Missing, *n*	4	3	1			

a Adjusted for centre, infant's age at randomisation and parity.
b According to maternal self-report, defined as any breastmilk feeding in the 24 hours prior to the infant reaching 3 months of age.

TABLE 10 Pre-specified subgroup analyses for the primary outcome (any breastmilk feeding at 3 months)

Primary outcome	Total (*n* = 169)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)
Infant's age at randomisation			
≥2 weeks			
Yes, *n* (%)	93 (92.1)	43 (91.5)	50 (92.6)
No, *n* (%)	8 (7.9)	4 (8.5)	4 (7.4)
Missing, *n*	4	3	1
<2 weeks			
Yes, *n* (%)	49 (79.0)	24 (82.8)	25 (75.8)
No, *n* (%)	13 (21.0)	5 (17.2)	8 (24.2)
Missing, *n*	2	1	1
Degree of tongue-tie (BTAT score) at randomisation			
≤4			
Yes, *n* (%)	46 (83.6)	23 (79.3)	23 (88.5)
No, *n* (%)	9 (16.4)	6 (20.7)	3 (11.5)
Missing, *n*	0	0	0
5–8			
Yes, *n* (%)	95 (88.8)	44 (93.6)	51 (85.0)
No, *n* (%)	12 (11.2)	3 (6.4)	9 (15.0)
Missing, *n*	6	4	2
Missing, *n*	1	0	1
Mother's prior beliefs about frenotomy			
Think it will help my baby			
Yes, *n* (%)	73 (88.0)	34 (87.2)	39 (88.6)
No, *n* (%)	10 (12.0)	5 (12.8)	5 (11.4)
Missing, *n*	3	2	1
Do not know if it will help my baby			
Yes, *n* (%)	66 (85.7)	32 (88.9)	34 (82.9)
No, *n* (%)	11 (14.3)	4 (11.1)	7 (17.1)
Missing, *n*	2	1	1
Think it is unlikely to help my baby			
Yes, *n* (%)	1 (100.0)	0 (0.0)	1 (100.0)
No, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
Missing, *n*	0	0	0
Missing, *n*	2	1	1
Recruited pre- or posttrial pause[a] during the COVID-19 pandemic			
Pre-pause			
Yes, *n* (%)	89 (87.3)	45 (91.8)	44 (83.0)

TABLE 10 Pre-specified subgroup analyses for the primary outcome (any breastmilk feeding at 3 months) (*continued*)

Primary outcome	Total (*n* = 169)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)
No, *n* (%)	13 (12.7)	4 (8.2)	9 (17.0)
Missing, *n*	5	3	2
Postpause			
Yes, *n* (%)	53 (86.9)	22 (81.5)	31 (91.2)
No, *n* (%)	8 (13.1)	5 (18.5)	3 (8.8)
Missing, *n*	1	1	0

a Trial paused recruitment on 17 March 2020 and resumed on 22 May 2020.

Pre-specified subgroup analyses

There were no notable differences between both the arms for any of the selected subgroups except that the rate of breastmilk feeding at 3 months appeared higher in the frenotomy with breastfeeding support arm compared to the breastfeeding support arm (92% vs. 83%) before the trial paused due to the coronavirus pandemic (see *Table 10*). After the trial restarted, the rate was higher in the breastfeeding support arm compared to the frenotomy with breastfeeding support arm (91% vs. 81%).

Secondary analyses

There were minimal differences between infants of mothers who complied with the intervention compared to non-compliers in the breastfeeding support arm for most baseline characteristics (see *Table 11*). However, a higher proportion of mothers who did not comply believed that frenotomy was helpful for their baby compared to mothers who complied (39/65, 61% vs. 6/24, 25%). A higher proportion of infants in the complier group had a BTAT score >4 compared to non-compliers (21/24, 88% vs. 41/64, 64%). The rate of breastmilk feeding at 3 months was higher among non-compliers compared to compliers (59/65, 91% vs. 16/24, 73%) (see *Table 12*), but the results from the CACE analysis showed no evidence for a difference in rates of breastmilk feeding at 3 months between the arms (RR 1.09, 95% CI 0.53 to 1.64) (see *Table 13*).

Economic evaluation

NHS health-care resource use

Tables 14 and *15* present health-care resource use associated with the intervention-related health-care resource use. *Table 14* presents the number of frenotomies performed from trial entry up to 3 months after birth across all participants. All frenotomies were performed by NHS providers, with 61 (76.25%) and 56 (62.9%) of procedures conducted by midwives in the frenotomy and no frenotomy groups, respectively. In the frenotomy with breastfeeding support group, 75 participants (93.75%) had the procedure whereas 65 participants (73.0%) had the procedure in the breastfeeding support group. Total numbers of frenotomies conducted across all participants in the trial are presented in *Appendix 2*, *Table 23*. *Table 15* reports the different types of breastfeeding support received up to 3 months of age across all participants. Different types of support services were accessed including the NHS infant feeding service and/or other breastfeeding support services. The latter included access to a breastfeeding café, the Breastfeeding Network, La Leche League, the NCT (formerly National Childbirth Trust) or contacts with any other trained breastfeeding supporter. *Table 24* reports the same information

TABLE 11 Characteristics of women and degree of tongue-tie by compliance status of breastfeeding support group arm

	Total (*n* = 89)	Non-complier (frenotomy performed) (*n* = 65)	Complier (frenotomy not performed) (*n* = 24)
Mother's age (years), mean (SD)	31.9 (5.1)	32.1 (4.8)	31.6 (5.8)
Missing, *n*	3	3	0
Mother's ethnic group			
White, *n* (%)	84 (95.5)	61 (95.3)	23 (95.8)
Asian, *n* (%)	2 (2.3)	1 (1.6)	1 (4.2)
Black, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
Mixed, *n* (%)	2 (2.3)	2 (3.1)	0 (0.0)
Other, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
Missing, *n*	1	1	0
Deprivation index			
1 (most deprived), *n* (%)	10 (11.2)	8 (12.3)	2 (8.3)
2, *n* (%)	18 (20.2)	14 (21.5)	4 (16.7)
3, *n* (%)	17 (19.1)	11 (16.9)	6 (25.0)
4, *n* (%)	25 (28.1)	17 (26.2)	8 (33.3)
5 (least deprived), *n* (%)	19 (21.4)	15 (23.1)	4 (16.7)
Previous live birth(s)[a]			
Yes, *n* (%)	42 (47.2)	32 (49.2)	10 (41.6)
No, *n* (%)	47 (52.8)	33 (50.8)	14 (58.3)
Breastfed before			
Yes, *n* (%)	40 (95.2)	30 (93.8)	10 (100.0)
No, *n* (%)	2 (4.8)	2 (6.2)	0 (0.0)
Not applicable – no previous live birth, *n*	47	33	14
Pre-trial breastfeeding support received			
Yes, *n* (%)	74 (84.1)	53 (82.8)	21 (87.5)
No, *n* (%)	14 (15.9)	11 (17.2)	3 (12.5)
Missing, *n*	1	1	0
Mother's pain while feeding during previous 24 hours,[b] **median (IQR)**	4 (2–7)	5 (2–7)	3.5 (0–6)
Missing, *n*	1	1	0
Mother's prior beliefs about frenotomy			
Think it will help my baby, *n* (%)	45 (51.1)	39 (60.9)	6 (25.0)
Do not know if it will help my baby, *n* (%)	42 (47.7)	25 (39.1)	17 (70.8)
Think it is unlikely to help my baby, *n* (%)	1 (1.1)	0 (0.0)	1 (4.2)
Missing, *n*	1	1	0

TABLE 11 Characteristics of women and degree of tongue-tie by compliance status of breastfeeding support group arm (*continued*)

	Total (*n* = 89)	Non-complier (frenotomy performed) (*n* = 65)	Complier (frenotomy not performed) (*n* = 24)
Maternal anxiety or depression[c]			
Yes, *n* (%)	40 (46.0)	30 (47.6)	10 (41.7)
No, *n* (%)	47 (54.0)	33 (52.4)	14 (58.3)
Missing, *n*	2	2	0
Maternal HRQoL,[d] **mean (SD)**	0.77 (0.16)	0.75 (0.14)	0.80 (0.20)
Missing, *n*	4	4	0
Recruited pre- or posttrial pause[e] **during the COVID-19 pandemic**			
Pre-pause, *n* (%)	55 (61.8)	35 (53.8)	20 (83.3)
Postpause, *n* (%)	34 (38.2)	30 (46.2)	4 (16.7)
Degree of tongue-tie (BTAT)			
0–4, *n* (%)	26 (30.0)	23 (35.9)	3 (12.5)
5–6, *n* (%)	32 (36.4)	24 (37.5)	8 (33.3)
7–8, *n* (%)	30 (34.1)	17 (26.6)	13 (54.2)
Missing, *n*	1	1	0

a Stratification factor.
b Measured using visual analogue scale of the SF-MPQ, modified into a 10-point Likert scale.
c Anxiety and depression dimension of EQ-5D-5L categorised into levels 2–5 (presence of anxiety/depression) and level 1 (no anxiety/depression).
d EQ-5D-5L overall index value.
e Trial paused recruitment on 17 March 2020 and resumed on 22 May 2020.

TABLE 12 Primary outcome by compliance status of breastfeeding support arm

	Total (*n* = 89)	Non-complier (frenotomy performed) (*n* = 65)	Complier (frenotomy not performed) (*n* = 24)
Any breastmilk feeding[a]			
Yes, *n* (%)	75 (86.2)	59 (90.8)	16 (72.7)
No, *n* (%)	12 (13.8)	6 (9.2)	6 (27.3)
Missing, *n*	2	0	2

a According to maternal self-report, defined as any breastmilk feeding in the 24 hours prior to the infant reaching 3 months of age.

as *Table 15* but only for those women who received breastfeeding support. There were no statistically significant differences in the breastfeeding support received between trial arms.

Maternal health-care resources consumed at 3 months of age is presented in *Table 16* across all participants. Similar information is presented in *Table 25* but the mean number of resources consumed is calculated only for those consuming the health-care resource use category. No significant differences for any resource use categories between groups were detected in any of the resource use categories: primary care, community care, secondary care and any other health-care professionals.

TABLE 13 Primary outcome for compliant groups (CACE analysis)

	Frenotomy w/ breastfeeding support (*n* = 76)		Breastfeeding support (*n* = 87)			
	Primary outcome	Event rate (%)	Compliance	Primary outcome[b]	Event rate (%)	CACE risk ratio (95% CI)[a]
Compliers	15/19	78.9	22 (25.3)	16/22	72.7	
Non-compliers	52/57	91.2	65 (74.7)	59/65	90.8	1.09 (0.53 to 1.64)
Total	67/76	88.2		75/87	86.2	

a The CI was calculated using bootstrapping.
b According to maternal self-report, defined as any breastmilk feeding in the 24 hours prior to the infant reaching three months of age.

TABLE 14 Number of frenotomies performed in the 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth

	Frenotomy with breastfeeding support (*n* = 80), *n* (%)	Breastfeeding support only (*n* = 89), *n* (%)
Frenotomies performed by a private provider	**0**	**0**
Frenotomies performed by the NHS provider	**75 (93.75%)**	**65 (73.0%)**
Doctor	13 (16.25%)	6 (6.7%)
Midwife	61 (76.25%)	56 (62.9%)
Other	1 (1.25%)	0
Missing	0	3 (3.4%)
Frenotomies with complications	1 (1.25%)	2 (2.2%)
Frenotomies not performed	**5 (6.25%)**	**24 (27.0%)**

TABLE 15 Breastfeeding support received in the 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across all participants

	Frenotomy with breastfeeding support (*n* = 80)		Breastfeeding support only (*n* = 89)		Mean difference in number of contacts (95% CI)[a]
	Number of patients (%)	Mean number of contacts (SD)	Number of patients (%)	Mean number of contacts (SD)	
Total breastfeeding support received	**50 (62.5)**	**2.53 (2.87)**	**60 (67.4)**	**2.69 (2.65)**	**−0.26 (−1.12 to 0.61)**
NHS contacts	43 (53.75)	1.62 (1.85)	49 (55.0)	2.07 (2.46)	−0.4 (−1.1 to 0.29)
Phone	26 (60.5)	0.72 (1.13)	32 (65.3)	0.73 (1.23)	
In person	29 (67.4)	0.9 (1.51)	37 (75.5)	1.33 (2.09)	
Missing	8 (10.0)	---	14 (15.73)	---	
Other contacts	18 (22.5)	0.9 (2.06)	15 (16.85)	0.59 (1.49)	0.18 (−0.39 to 0.75)
Phone	9 (50.0)	0.39 (1.23)	12 (75.0)	0.38 (1.18)	
In person	14 (77.8)	0.51 (1.31)	10 (62.5)	0.22 (0.73)	
Missing	8 (10.0)	---	15 (16.58)	---	
Not received	22 (27.5)	---	14 (15.73)	---	

a Adjusted for centre, infant's age at randomisation and parity.

TABLE 16 Maternal health-care resource use by category and item between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across all participants

Resource use category and item	Frenotomy with breastfeeding support (*n* = 80)		Breastfeeding support only (*n* = 89)		
	Number of participants (%)	Mean number of contacts[a] (SD)	Number of participants (%)	Mean number of contacts[a] (SD)	Mean difference in number of contacts (95% CI)[a]
Primary care					
General practitioner visits	73 (91.25)	0.92 (1.05)	73 (82.0)	0.64 (0.95)	0.26 (−0.07 to 0.58)
Yes	73 (91.25)		73 (82.0)		
No	0		0		
Missing	7 (8.75)	---	16 (18.0)	---	
Practice nurse visits	73 (91.25)	0.16 (0.94)	74 (83.15)	0.11 (0.48)	0.07 (−0.19 to 0.33)
Yes	73 (91.25)		74 (83.15)		
No	0		0		
Missing	7 (8.75)	---	15 (16.85)	---	
Medicines	73 (91.25)	0.29 (0.72)	74 (83.15)	0.15 (0.51)	0.17 (−0.03 to 0.37)
Yes	14 (17.5)		7 (7.9)		
No	59 (73.75)		67 (75.25)		
Missing	7 (8.75)	---	15 (16.85)	---	
Of which antibiotics	73 (91.25)	0.25 (0.6)	74 (83.15)	0.12 (0.47)	
Yes	13 (16.25)		6 (6.7)		
No	60 (75.0)		68 (76.45)		
Missing	7 (8.75)	---	15 (16.85)	---	
Of which for anxiety/ depression	73 (91.25)	0.04 (0.26)	74 (83.15)	0.03 (0.16)	
Yes	2 (2.5)		2 (2.2)		
No	71 (88.75)		72 (80.95)		
Missing	7 (8.75)	---	15 (16.85)	---	
Community care					
Community nurse/ midwife contacts	73 (91.25)	0.07 (0.35)	74 (83.15)	0.04 (0.26)	−0.01 (−0.1 to 0.08)
Yes	3 (3.75)		2 (2.2)		
No	70 (87.5)		72 (80.95)		
Missing	7 (8.75)	---	15 (16.85)	---	
Of which virtual	73 (91.25)	0 (0)	74 (83.15)	0.013 (0.116)	
Yes	0		1 (1.15)		
No	73 (91.25)		73 (82.0)		
Missing	7 (8.75)	---	15 (16.85)	---	
Of which in person	73 (91.25)	0.07 (0.35)	74 (83.15)	0.03 (0.16)	

continued

TABLE 16 Maternal health-care resource use by category and item between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across all participants (*continued*)

Resource use category and item	Frenotomy with breastfeeding support (*n* = 80)		Breastfeeding support only (*n* = 89)		
	Number of participants (%)	Mean number of contacts[a] (SD)	Number of participants (%)	Mean number of contacts[a] (SD)	Mean difference in number of contacts (95% CI)[b]
Yes	3 (3.75)		2 (2.2)		
No	70 (87.5)		72 (80.95)		
Missing	7 (8.75)	---	15 (16.85)	---	
Secondary (hospital-based) care					
Accident & emergency department visits	73 (91.25)	0.027 (0.234)	74 (83.15)	0.013 (0.116)	0.004 (−0.057 to 0.065)
Yes	1 (1.25)		1 (1.15)		
No	72 (90.0)		73 (82.0)		
Missing	7 (8.75)	---	15 (16.85)	---	
Hospital outpatient clinic appointments	73 (91.25)	0.14 (0.51)	74 (83.15)	0.05 (0.37)	0.07 (−0.08 to 0.22)
Yes	6 (7.5)		2 (2.2)		
No	67 (83.75)		72 (80.95)		
Missing	7 (8.75)	---	15 (16.85)	---	
Of which virtual	73 (91.25)	0.03 (0.23)	74 (83.15)	0 (0)	
Yes	1 (1.25)		0		
No	72 (90.0)		74 (83.15)		
Missing	7 (8.75)	---	15 (16.85)	---	
Of which in person	73 (91.25)	0.11 (0.39)	74 (83.15)	0.05 (0.37)	
Yes	6 (7.5)		2 (2.2)		
No	67 (83.75)		72 (80.95)		
Missing	7 (8.75)	---	15 (16.85)	---	
Hospital admissions	72 (90.0)	0.014 (0.118)	75 (84.25)	0.013 (0.115)	0.015 (−0.013 to 0.044)
Yes	1 (1.25)		1 (1.1)		
No	71 (88.75)		74 (83.15)		
Missing	8 (10.0)	---	14 (15.75)	---	
Length of stay (days)		0.014 (0.118)		0.027 (0.231)	0.015 (−0.013 to 0.044)
Missing	8 (10.0)	---	14 (15.7)	---	
Any other NHS health-care professionals contacts					
Other NHS health-care professionals contacts	73 (91.25)	0.19 (0.64)	74 (83.15)	0.16 (0.66)	0.03 (−0.19 to 0.25)
Yes	7 (8.75)		5 (5.5)		
No	66 (82.5)		69 (77.5)		

TABLE 16 Maternal health-care resource use by category and item between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across all participants (*continued*)

Resource use category and item	Frenotomy with breastfeeding support (*n* = 80)		Breastfeeding support only (*n* = 89)		
	Number of participants (%)	Mean number of contacts[a] (SD)	Number of participants (%)	Mean number of contacts[a] (SD)	Mean difference in number of contacts (95% CI)[b]
Missing	7 (8.75)	---	15 (16.85)	---	
Of which virtual	73 (91.25)	0.05 (0.33)	74 (83.15)	0.09 (0.58)	
Yes	2 (2.5)		2 (2.2)		
No	71 (88.75)		72 (80.95)		
Missing	7 (8.75)	---	15 (16.85)	---	
Of which in person	73 (91.25)	0.14 (0.45)	74 (83.15)	0.07 (0.34)	
Yes	7 (8.75)		3 (3.35)		
No	66 (82.5)		71 (79.8)		
Missing	7 (8.75)	---	15 (16.85)	---	
Any other non-NHS health-care professionals contacts					
Osteopath visits	73 (91.25)	0 (0)	74 (83.15)	0.07 (0.42)	−0.07 (−0.17 to 0.03)
Yes	0		2 (2.2)		
No	73 (91.25)		72 (80.95)		
Missing	7 (8.75)	---	15 (16.85)	---	

a Mean number of courses received in the medicines and mean number of hospital admissions in the hospital admissions.
b Adjusted for centre, infant's age at randomisation, and parity.

Table 17 presents health-care resource utilization for infants from trial entry up to 3 months across all participants in the study. *Table 26* presents health-care utilization but only for those infants consuming the health-care resource use category. Similar to maternal health-care utilization, we did not observe any mean differences in visits for any of the categories: primary care, community care, secondary care and any other health-care professionals.

NHS health-care costs

Table 18 reports the cost analysis results for mothers and their babies over the study period. A borderline statistically significant mean cost difference (95% CI) of £27 (£0.3–54) between groups favouring the frenotomy was observed in the intervention-related costs. There were no significant differences in any cost categories incurred by mothers or their babies between the frenotomy with breastfeeding support and breastfeeding support groups. The mean (SD) total cost per woman/infant pair was estimated to be £497 (£854) and £483 (£529) in the frenotomy and no frenotomy groups, respectively, and a non-significant mean cost difference (95% CI) of £21 (−£221 to £263) was detected. Maternal and infant cost analysis across all participants in the study is presented in *Table 27*.

Maternal HRQoL using EQ-5D-5L instrument

The distribution of response across all EQ-5D-5L dimensions at different follow-ups are presented in *Table 28*. A significant difference in the distribution of responses between groups was observed at

TABLE 17 Infants health-care resource use by category and item between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across all participants

Resource use category and item	Frenotomy with breastfeeding support (*n* = 80)		Breastfeeding support only (*n* = 89)		
	Number of patients (%)	Mean number of contacts[a] (SD)	Number of patients (%)	Mean number of contacts[a] (SD)	Mean difference in number of contacts (95% CI)[a]
Primary care					
General practitioner contacts	73 (91.25)	0.86 (0.92)	72 (80.9)	0.86 (1.12)	0.03 (−0.30 to 0.37)
Yes	42 (52.5)		37 (41.6)		
No	31 (38.75)		35 (39.3)		
Missing	7 (8.75)	---	17 (19.10)	---	
Of which virtual	73 (91.25)	0 (0)	72 (80.9)	0.014 (0.083)	
Yes	0		1 (1.1)		
No	73 (91.25)		71 (79.8)		
Missing	7 (8.75)	---	17 (19.10)	---	
Of which in person	73 (91.25)	0.86 (0.92)	72 (80.9)	0.85 (1.1)	
Yes	42 (52.5)		37 (41.6)		
No	31 (38.75)		35 (39.3)		
Missing	7 (8.75)	---	17 (19.10)	---	
Practice nurse visits	73 (91.25)	0.12 (0.47)	74 (83.15)	0.13 (0.48)	−0.02 (−0.19 to 0.14)
Yes	5 (6.25)		6 (6.75)		
No	68 (85.0)		68 (76.4)		
Missing	7 (8.75)	---	15 (16.85)	---	
Medicines (antibiotics)	73 (91.25)	0.05 (0.23)	74 (83.15)	0.08 (0.27)	−0.03 (−0.11 to 0.06)
Yes	4 (5.0)		6 (6.75)		
No	69 (86.25)		68 (76.4)		
Missing	7 (8.75)	---	15 (16.85)	---	
Community care					
Community nurse/midwife visits	73 (91.25)	0.11 (0.94)	74 (83.15)	0.03 (0.16)	0.08 (−0.15 to 0.30)
Yes	1 (1.25)		2 (2.2)		
No	72 (90.0)		72 (80.95)		
Missing	7 (8.75)	---	15 (16.85)	---	
Infant health visitor contacts	72 (90.0)	0.25 (1.0)	74 (83.15)	0.19 (0.65)	0.07 (−0.22 to 0.36)
Yes	5 (6.25)		7 (7.9)		
No	67 (83.75)		67 (75.25)		
Missing	8 (10.0)	---	15 (16.85)	---	

TABLE 17 Infants health-care resource use by category and item between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across all participants (*continued*)

Resource use category and item	Frenotomy with breastfeeding support (*n* = 80)		Breastfeeding support only (*n* = 89)		
	Number of patients (%)	Mean number of contacts[a] (SD)	Number of patients (%)	Mean number of contacts[a] (SD)	Mean difference in number of contacts (95% CI)[a]
Of which virtual	72 (90.0)	0.08 (0.71)	74 (83.15)	0.01 (0.12)	
Yes	1 (1.25)		1 (1.1)		
No	71 (88.75)		73 (82.05)		
Missing	8 (10.0)	---	15 (16.85)	---	
Of which in-person	72 (90.0)	0.17 (0.73)	74 (83.15)	0.18 (0.63)	
Yes	4 (5.0)		7 (7.9)		
No	68 (85.0)		67 (75.25)		
Missing	8 (10.0)	---	15 (16.85)	---	
Community paediatrician visits	73 (91.25)	0.01 (0.12)	74 (83.15)	0.03 (0.16)	−0.02 (−0.07 to 0.03)
Yes	1 (1.25)		2 (2.2)		
No	72 (90.0)		72 (80.95)		
Missing	7 (8.75)	---	15 (16.85)	---	
Secondary (hospital-based) care					
Accident & emergency department visits	73 (91.25)	0.07 (0.3)	74 (83.15)	0.04 (0.2)	0.03 (−0.06 to 0.12)
Yes	4 (5.0)		3 (3.35)		
No	69 (86.25)		71 (79.8)		
Missing	7 (8.75)	---	15 (16.85)	---	
Hospital outpatient clinic appointments	73 (91.25)	0.16 (0.96)	74 (83.15)	0.04 (0.26)	0.12 (−0.12 to 0.36)
Yes	5 (6.25)		2 (2.2)		
No	68 (85.0)		72 (80.95)		
Missing	7 (8.75)	---	15 (16.85)	---	
Hospital admissions	72 (90.0)	0.1 (0.51)	75 (84.25)	0.13 (0.38)	−0.03 (−0.18 to 0.11)
Yes	4 (5.0)		9 (10.1)		
No	68 (85.0)		66 (74.15)		
Missing	8 (10.0)	---	14 (15.75)	---	
Length of stay (days)		0.33 (2.16)		0.24 (0.75)	0.14 (-0.38 to 0.67)
Missing	8 (10.0)	---	14 (15.75)	---	
Any other NHS health-care professionals visits					
Other NHS health-care professionals visits	72 (90.0)	0.05 (0.37)	72 (80.95)	0.04 (0.26)	0.01 (−0.09 to 0.12)

continued

TABLE 17 Infants health-care resource use by category and item between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across all participants (*continued*)

Resource use category and item	Frenotomy with breastfeeding support (*n* = 80)		Breastfeeding support only (*n* = 89)		
	Number of patients (%)	Mean number of contacts[a] (SD)	Number of patients (%)	Mean number of contacts[a] (SD)	Mean difference in number of contacts (95% CI)[b]
Yes	2 (2.5)		2 (2.2)		
No	70 (87.5)		70 (78.75)		
Missing	8 (10.0)	---	17 (19.05)	---	
Any other non-NHS health-care professionals visits					
Osteopath visits	72 (90.0)	0.04 (0.26)	72 (80.95)	0.11 (0.49)	−0.07 (−0.21 to 0.07)
Yes	2 (2.5)		4 (4.55)		
No	70 (87.5)		68 (76.4)		
Missing	8 (10.0)	---	17 (19.05)	---	

a Mean number of courses received in the medicines and mean number of hospital admissions in the hospital admissions.
b Adjusted for centre, infant's age at randomisation, and parity.

the routine follow-up visit for the mobility dimension (χ^2 = 10.429 with *p*-value of 0.005). No other significant difference was observed in any of the other dimensions. *Table 19* presents the results of the HRQoL analysis between trial arms at different follow-up points. The mean (SD) HRQoL at baseline was 0.773 (0.179) and 0.766 (0.162), at routine follow-up was 0.851 (0.141) and 0.824 (0.157) and at 3 months after birth was 0.850 (0.183) and 0.868 (0.117) in the frenotomy and no frenotomy groups, respectively. No statistically significant mean differences were detected in overall HRQoL at baseline, routine follow-up and 3 months after birth.

Maternal QALYs

Table 20 shows QALDs and QALYs between trial arms at 3 months of age. The mean (SD) QALYs was estimated to be 0.2117 (0.0345) and 0.2099 (0.0303) in the frenotomy with breastfeeding support and breastfeeding support groups, respectively. There were no significant mean differences in QALDs or QALYs between the frenotomy with breastfeeding support and breastfeeding support groups.

Cost-utility analysis

A summary of cost-effectiveness results comparing frenotomy with breastfeeding support with breastfeeding support only is presented in *Table 21*. This analysis was undertaken using a complete-case analysis with pairs of total costs and QALYs available for each trial participant. The ICER was estimated to be £6113 per QALY gained indicating that such point estimate is below current thresholds of willingness to pay for QALY gained of £20,000. However, *Figure 2* displays the uncertainty around the ICER on the CEP with the joint distribution of mean differences in costs and QALYs. The chart clearly shows bootstrap replicates expanding the four quadrants of the plane indicating that CIs for the ICER in this case would be misleading and difficult to interpret. More informative is *Figure 3* that suggests that at a threshold of £20,000 per QALY gained, frenotomy only reaches 50% probability of being cost-effective. Increasing this willingness to pay above that value tends asymptotically towards 60% of being cost-effective.

TABLE 18 Maternal and infant cost analysis between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across all participants (expressed in 2019/2020 UK pounds sterling)

Resource use category and item	Frenotomy with breastfeeding support (*n* = 80), mean (SD)		Breastfeeding support only (*n* = 89), mean (SD)		Mean cost difference[a] (95% CI)	
	Mother	Infant	Mother	Infant	Mother	Infant
Frenotomy [1]		**£120 (£74)**		**£94 (£97)**		**£27 (£0.3 to £54)**
Missing, n (%)		0		0		---
Breastfeeding support						
NHS contacts, phone	£33 (£52)		£34 (£57)		£2 (−£16 to £20)	
NHS contacts, in person	£73 (£122)		£108 (£170)		−£36 (−£80 to £8)	
Total NHS contacts, breastfeeding support [2]	**£106 (£131)**		**£142 (£180)**		**−£34 (−£83 to £14)**	
Missing, n (%)	8 (10.0)		14 (16.0)			
Primary care						
General practitioner visits	£36 (£41)	£34 (£36)	£25 (£37)	£33 (£43)	£10 (−£3 to £23)	£2 (−£11 to £15)
Missing, n (%)	7 (8.75)	7 (8.75)	16 (18.0)	17 (19.1)		
Practice nurse visits	£1.8 (£10.4)	£1.4 (£5.2)	£1.2 (£5.3)	£1.5 (£5.2)	£0.7 (−£2.1 to £3.6)	−£0.3 (−£2.0 to £1.5)
Missing, n (%)	7 (8.75)	7 (8.75)	15 (16.85)	15 (16.85)		
Primary care, total	£38 (£43)	£35 (£36)	£27 (£39)	£35 (£43)	£10 (−£3 to £24)	£2 (−£12 to £15)
Missing, n (%)	7 (8.75)	7 (8.75)	17 (19.1)	18 (20.2)		
Primary care, total mother/infant pair [3]	**£73 (£65)**		**£62 (£67)**		**£11 (-£11 to £34)**	
Missing, n (%)	7 (8.75)		18 (20.2)			
Medicines						
Antibiotics	£1.6 (£8.0)	£0.2 (£1.0)	£0.5 (£2.2)	£0.3 (£1.2)	£1.2 (−£0.7 to £3.2)	−£0.1 (−£0.5 to £0.3)
For anxiety/depression	£0.3 (£2.4)	---	£0.1 (£0.4)	---	£0.3 (−£0.3 to £0.9)	
Medicines, total	£2.0 (£10.2)	£0.2 (£1.0)	£0.6 (£2.3)	£0.3 (£1.2)	£1.6 (−£1.0 to £4.1)	−£0.1 (−£0.5 to £0.3)

continued

TABLE 18 Maternal and infant cost analysis between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across all participants (expressed in 2019/2020 UK pounds sterling) (*continued*)

Resource use category and item	Frenotomy with breastfeeding support (*n* = 80), mean (SD)		Breastfeeding support only (*n* = 89), mean (SD)		Mean cost difference (95% CI)	
	Mother	Infant	Mother	Infant	Mother	Infant
Missing, n (%)	7 (8.75)	7 (8.75)	15 (16.85)	15 (16.85)		
Medicines, total mother/infant pair [4]	**£2.2 (£10.2)**		**£0.9 (£2.7)**		**£1.4 (−£1.1 to £4.0)**	
Missing, n (%)	7 (8.75)		15 (16.85)			
Community care						
Community nurse/midwife contacts	£3 (£16)	£9 (£79)	£2 (£10)	£2 (£14)	−£0.2 (−£4 to £4)	£6 (−£13 to £26)
Missing, n (%)	7 (8.75)	7 (8.75)	15 (16.85)	15 (16.85)		
Infant Health visitor contacts	---	£17 (£67)	---	£15 (£52)	---	£3 (−£17 to £23)
Missing, n (%)	---	8 (10.0)	---	15 (16.85)		
Community paediatrician visits	---	£5 (£41)	---	£10 (£57)	---	−£7 (−£24 to £9)
Missing, n (%)	---	7 (8.75)	---	15 (16.85)		
Community care, total	£3 (£16)	£27 (£116)	£2 (£10)	£27 (£79)	−£0.2 (−£4 to £4)	−£1 (−£33 to £33)
	7 (8.75)	8 (10.0)	15 (16.85)	15 (16.85)		
Community care, total mother/infant pair [5]	**£30 (£116)**		**£28 (£79)**		**−£1 (−£34 to £33)**	
Missing, n (%)	8 (10.0)		15 (16.85)			
Secondary (hospital-based) care						
Accident & emergency department visits	£5 (£43)	£12 (£55)	£2 (£21)	£7 (£36)	£1 (−£10 to £12)	£5 (−£10 to £21)
Missing, n (%)	7 (8.75)	7 (8.75)	15 (16.85)	15 (16.85)		
Hospital outpatient clinic appointments	£20 (£71)	£38 (£221)	£9 (£60)	£9 (£60)	£8 (−£14 to £30)	£27 (−£27 to £82)
Missing, n (%)	7 (8.75)	7 (8.75)	15 (16.85)	15 (16.85)		
Hospital admissions	£21 (£182)	£54 (£285)	£9 (£77)	£79 (£230)	£23 (−£21 to £68)	−£23 (−£106 to £59)
Missing, n (%)	8 (10.0)	8 (10.0)	14 (16.0)	14 (16.0)		

TABLE 18 Maternal and infant cost analysis between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across all participants (expressed in 2019/2020 UK pounds sterling) (*continued*)

Resource use category and item	Frenotomy with breastfeeding support (*n* = 80), mean (SD)		Breastfeeding support only (*n* = 89), mean (SD)		Mean cost difference[a] (95% CI)	
	Mother	Infant	Mother	Infant	Mother	Infant
Secondary (hospital-based) care, total	£47 (£202)	£105 (£540)	£20 (£99)	£97 (£252)	£33 (−£19 to £85)	£8 (−£130 to £146)
Missing, n (%)	8 (10.0)	8 (10.0)	15 (16.85)	15 (16.85)		
Secondary (hospital-based) care, total mother/infant pair [6]	**£152 (£568)**		**£117 (£299)**		**£42 (-£108 to £191)**	
Missing, n (%)	8 (10.0)		15 (16.85)			
Any other NHS health-care professionals contacts						
Other NHS health-care professionals contacts, total	£17 (£59)	£7 (£44)	£26 (£160)	£4 (£25)	−£10 (−£52 to £32)	£4 (−£8 to £16)
Missing, n (%)	7 (8.75)	7 (8.75)	15 (16.85)	15 (16.85)		
Other NHS health-care professionals contacts, total mother/infant pair [7]	**£25 (£83)**		**£30 (£164)**		**-£6 (-£51 to £39)**	
Missing, n (%)	7 (8.75)		15 (16.85)			
Any other non-NHS health-care costs						
Payment for anything to help breastfeeding	£3 (£9)	---	£11 (£35)	---	−£8 (−£17 to £1)	---
Missing, n (%)	13 (16.25)		18 (20.22)			
Non-NHS health-care professionals visits, osteopath	0 (0)	£2 (£12)	£3 (£20)	£5 (£23)	−£3 (−£8 to £2)	−£3 (−£10 to £3)
Missing, n (%)	7 (8.75)	8 (10.0)	15 (16.85)	17 (19.1)		
Other non-NHS health-care costs, total mother/infant pair [8]	**£5 (£18)**		**£20 (£52)**		**−£16 (−£29 to −£2)**	
Missing, n (%)	13 (16.25)		21 (23.6)			
Total maternal/infant costs [1] + [2] + [3] + [4] + [5] + [6] + [7]	**£215 (£274)**	**£285 (£745)**	**£218 (£312)**	**£262 (£349)**	**−£1 (−£99 to £98)**	**£31 (−£166 to £227)**
Missing, n (%)	9 (11.2)	9 (11.2)	17 (19.1)	18 (20.2)		
Total cost mother/infant pair [1] + [2] + [3] + [4] + [5] + [6] + [7]	**£497 (£854)**		**£483 (£529)**		**£21 (−£221 to £263)**	
Missing, n (%)	10 (12.5)		18 (20.2)			

a Adjusted for centre, infant's age at randomisation and parity.

TABLE 19 HRQoL at relevant time points trial period between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups

	Frenotomy with breastfeeding support (*n* = 80)	Breastfeeding support only (*n* = 89)	Mean difference[a] (95% CI)
HRQoL at baseline (trial entry)			
Mean (SD)	0.773 (0.179)	0.766 (0.162)	0.001 (−0.051 to 0.054)
Missing, n (%)	4 (5.0)	4 (4.5)	
HRQoL at routine follow-up (approximately 1 to 2 weeks posttrial entry)			
Mean (SD)	0.851 (0.141)	0.824 (0.157)	0.028 (−0.019 to 0.075)
Missing, n (%)	6 (7.5)	4 (4.5)	
HRQoL at 3 months after birth			
Mean (SD)	0.850 (0.183)	0.868 (0.117)	−0.018 (−0.072 to 0.032)
Missing, n (%)	8 (10.0)	15 (16.85)	

a Adjusted for centre, infant's age at randomisation and parity.

TABLE 20 Maternal QALYs and QALDs over trial period between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups

	Frenotomy with breastfeeding support (*n* = 80), mean (SD)	Breastfeeding support only (*n* = 89), mean (SD)	Mean difference[a] (95% CI)
QALDs			
Mean (SD)	77.12 (13.58)	76.47 (11.03)	0.55 (−3.46 to 4.56)
Missing, n (%)	11 (13.75)	15 (16.85)	
QALYs			
Mean (SD)	0.2117 (0.0345)	0.2099 (0.0303)	0.0015 (−0.0095 to 0.0125)
Missing, n (%)	11 (13.75)	15 (16.85)	

a Adjusted for centre, infant's age at randomisation and parity.

TABLE 21 Summary of CUA result using complete-case analysis

Trial arm	Total number of complete cases	Total costs (2019/2020 UK £), mean (SE)	Incremental costs, mean (SE)	QALYs, mean (SE)	Incremental QALYs, mean (SE)
Breastfeeding support only	66	488 (63)	---	0.2082 (0.0036)	---
Frenotomy with breastfeeding support	71	502 (106)	14 (123)	0.2105 (0.0043)	0.0023 (0.0056)

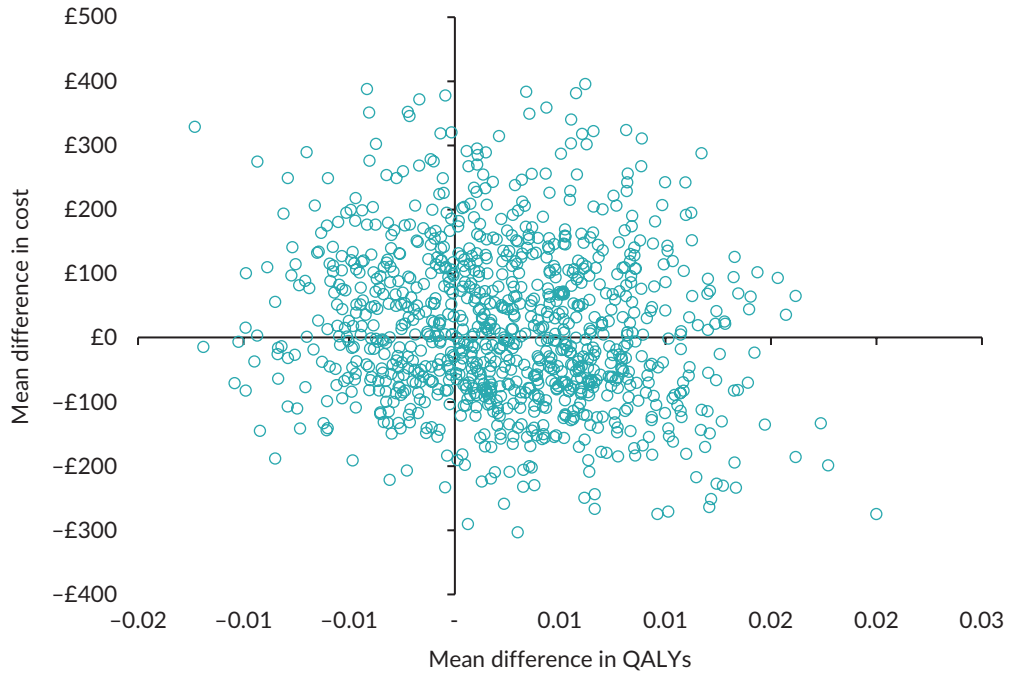

FIGURE 2 Bootstrap replications of mean difference in costs and effects plotted on the CEP.

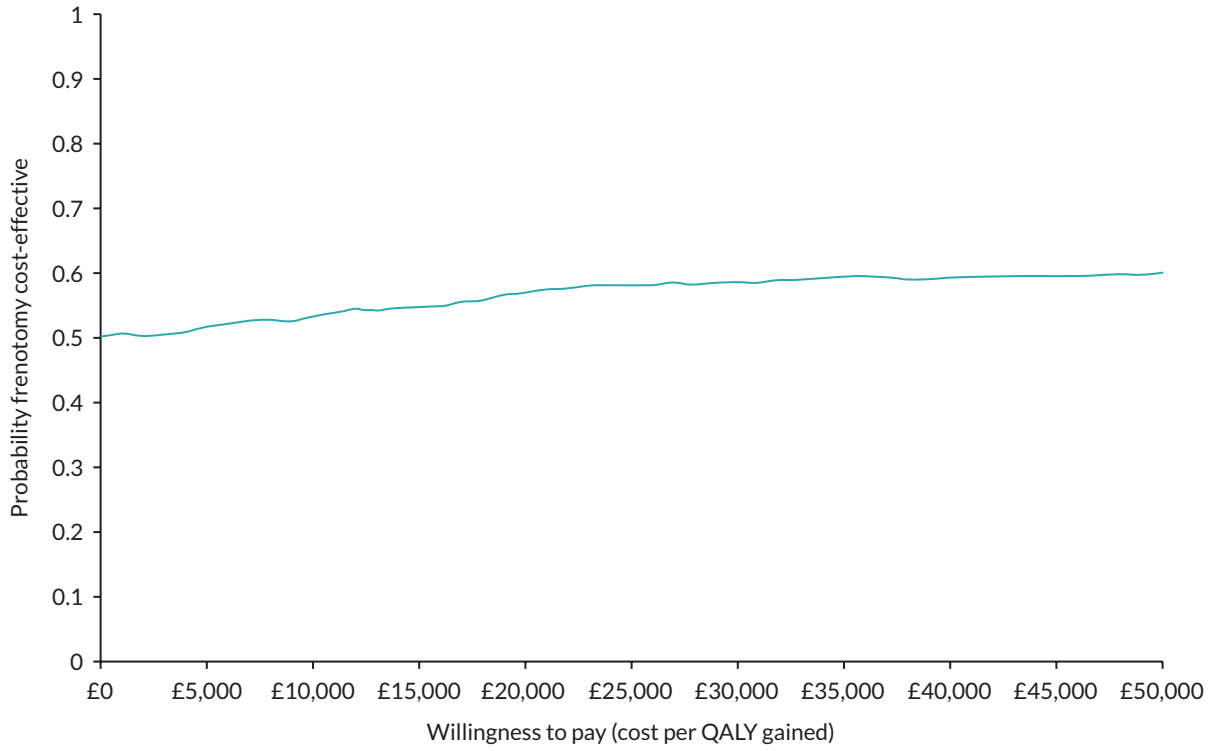

FIGURE 3 Cost-effectiveness acceptability curves indicating the probability that frenotomy is cost-effective compared to breastfeeding support only.

Site monitoring: barriers and facilitators to recruitment

Main factors identified in sites where recruitment was challenging

Several factors were identified, which represented barriers to trial recruitment, mostly related to equipoise among staff and women, but others concerning location and composition of recruiting teams.

Approaching women when they have already received breastfeeding support. In many areas capacity within infant feeding clinics and/or care pathways meant that women attended their first appointment only after they had been having difficulties with breastfeeding for some time. Only a third of babies recruited were <2 weeks old at trial entry (see *Table 1*). Many women felt that they had therefore already tried breastfeeding support without success, and therefore either were not willing to be randomised, or, if they were randomised to the breastfeeding support arm, they were willing only to try breastfeeding support alone for a few days before requesting frenotomy. Some sites gave women in the breastfeeding support arm 'just in case' appointments for frenotomy to address this concern, which had the effect of encouraging crossovers.

In the context of the pandemic, this was exacerbated, since parents were generally less willing to risk having to return for another clinic appointment and/or frenotomy when services were reduced, waiting times were longer and there were concerns over potential COVID-19 exposure by additional visits.

Sites that covered large geographical areas. Women who lived in remote areas wanted their baby to have a frenotomy before they left hospital or within the community so that they did not have to travel. The research team often did not therefore get to see the women before the procedure was carried out or they were discharged. This was a particular issue at one site where up to 10 midwives were qualified to perform a frenotomy. Their numbers of frenotomies performed were high and were often carried out on wards and within homes before there had been time to fully assess the need for a frenotomy and was associated with a lack of equipoise.

Online information regarding tongue tie. Once a diagnosis of tongue-tie has been suggested there is a substantial amount of pro-frenotomy information available online as well as chat groups suggesting that it is the magic fix to breastfeeding issues.

Lack of cohesion among the various professional teams. Often there were difficulties between ward-based research teams and community midwifery teams. Because women are now discharged from hospitals very early following delivery the community midwives are most often the ones to offer breastfeeding support within women's homes, unless they have frequent feeding support clinics provided by the Trust. In an ideal scenario they would be the ones best placed to recruit women to the trial. However, their caseloads are such that they do not have the time to include this within their practice and most are not research active and have not completed GCP training. Some breastfeeding support midwives who run clinics were willing to undergo training and did recruit to the trial. Some community teams were willing to hand out FROSTTIE leaflets, some were not.

Gatekeeping. One site that withdrew from the trial had a single member of staff who controlled the flow of women coming to the frenotomy clinic appointments and who refused to refer women to the research team. Some clinics were also set in remote sites away from the research team, which made recruitment challenging.

The naming of clinics. If women were invited to attend a tongue-tie clinic then they were expecting to receive a frenotomy for their babies. Feeding support clinics seemed to recruit better.

Lack of feeding support clinics. Some sites had very few clinics, for example just one 4-hour clinic per week. There was a major lack of funding for breastfeeding support services at all sites.

Frenotomies being performed within a different department to the feeding support clinics. Sometimes there was only one member of staff trained to perform frenotomies. This was particularly difficult in one hospital when the service ceased due to long-term sickness. Recruitment was also challenging if the frenotomy teams had no breastfeeding support experience, for example if they were maxillofacial surgery teams.

Feeding support clinics held in a different location to the research teams. This meant that a member of the research team either had to wait throughout the clinic for a potentially eligible recruit, which prevented them from working on other trials, or they had to drop everything and travel to a satellite site at short notice. Many women were not willing to wait for a member of the research team to arrive in this situation. Related to this there was felt, in some sites, to be a lack of funding for research midwife hours.

Paediatric research nurses or research practitioners appointed to cover FROSTTIE as opposed to research midwives. In sites where there was a lack of cohesion between the groups (midwives and nurses identifying as very different professional groups), this caused some issues with cooperation between community staff and research staff.

Research staff time limitations. Research staff did not generally cover weekends within the hospitals, only worked office hours and in some cases only provided cover 3 or 4 days per week. This obviously impacted on recruitment and even more so during annual leave and sickness.

Main factors identified at successful recruiting sites

These were often, not always, the converse of those observed at sites where recruitment was challenging, and showed that recruitment within hospital settings was possible.

Clinics named 'feeding' or 'breastfeeding support' clinics.

Frequent clinics, some offering drop-in clinics up to 5 days per week.

Trial 'fit' with their current practice. For example, sites where women and their babies were assessed and if found to have a tongue tie and feeding difficulties they **would not** be automatically referred to a frenotomy clinic. They would be sent home to try changes in positioning prior to being re-assessed and possibly then referred for frenotomy.

Recruited early. Babies were recruited at the point of first contact within the clinics prior to breastfeeding support.

Cohesive teams. Clinics for support and frenotomy were held within the same department. Research teams had a good relationship with the feeding support midwives and those who perform the frenotomy.

Pandemic changes to services

In several areas the onset of the COVID-19 pandemic saw the withdrawal of breastfeeding support services, either in person or at all. In areas where all support was withdrawn, as Trusts did not consider breastfeeding support to be an essential service, the trial had to stop. Similarly in some areas frenotomy lists ceased. Other areas moved to providing a remote breastfeeding support service with subsequent frenotomy if necessary, and it was suggested that the trial could move to a centralised model providing fully remote breastfeeding support with referral for frenotomy for those randomised. This would have had the added benefit of enabling breastfeeding support for women in areas where support had been withdrawn and could have enhanced recruitment, but at the time was not considered an appropriate change by the funder.

Chapter 4 Discussion and conclusions

Summary of main findings

The trial did not reach its pre-specified sample size and there was no evidence of differences between trial arms in any outcomes. Rates of continued breastmilk feeding were high at 3 months in both the frenotomy with breastfeeding support and breastfeeding support groups. Compared to first follow-up, pain during breastfeeding was lower at 3 months in both groups. Complications of the procedure were not uncommon, occurring in around 1 in 50 infants. There was a high rate of crossover between arms with 73% of babies in the breastfeeding support arm undergoing frenotomy. Almost two-thirds of women in the breastfeeding support without frenotomy arm whose babies went on to have a frenotomy believed at recruitment that a frenotomy would benefit their child, indicating clear evidence of lack of equipoise. A higher proportion of infants in the non-complier group had a BTAT score of 4 or below, indicating a more restricted tongue compared to compliers. Substantial uncertainty still remains about whether frenotomy with breastfeeding support is a cost-effective use of NHS resources compared with breastfeeding support only.

Limitations

The statistical power of the analysis was extremely limited due to not achieving the target sample size because of the early cessation of the trial and the high proportion of infants in the breastfeeding support arm who underwent frenotomy. Mothers recruited to the trial were more likely to be older, less likely to be of minority ethnicity and more likely to live in more affluent areas than the general population of women giving birth in the UK,[6] which may further limit generalisability of the findings.

Comparison with the existing literature

Most infants in the control groups of the five previous trials identified in the Cochrane review[12] also underwent frenotomy. Two studies offered frenotomy to all participants, and the other three trials, most of which compared frenotomy to standard care, reported frenotomy rates between 77% and 97%. On this basis all five trials were considered of low quality and at high risk of bias. The 73% frenotomy rate in the breastfeeding support arm that we observed in FROSTTIE is therefore very comparable, but on this basis it must also be regarded as at high risk of bias. The Cochrane review authors concluded that, in the settings where these trials were carried out, equipoise concerning frenotomy was lacking, and FROSTTIE echoes this. Equipoise was a barrier to recruitment due to both staff attitudes and parents' expectations. Staff broadly fell into two groups. The first group felt strongly that frenotomy was an important intervention, which might aid breastfeeding, and as it had minimal risk of harm should not be denied to women whose babies were diagnosed with tongue-tie and who had breastfeeding difficulties. These staff were reluctant to randomise infants unless the infants were very young, that is before breastfeeding had really been established. It is important to note that although the Cochrane review did not identify any complications of the procedure among the 302 included infants,[12] three infants in the FROSTTIE trial had significant complications (bleeding or salivary duct damage), around 1 in every 50 infants. Others have noted concerns over the potential harms of the procedure when its benefits have not been established in high-quality trials.[34]

The second group of staff were very clear that expert breastfeeding support was the most important part of the intervention to assist with breastfeeding difficulties and recognised that frenotomy was not without potential harm. These staff were not willing to randomise infants to possible frenotomy until they had a substantial period of breastfeeding support, at which point women themselves were less

willing to be randomised as they were desperate for any intervention which might help. Almost all staff fell into one of these two groups with few staff opinions in between.

As evidenced from *Tables 2* and *11*, which show that more than half of women recruited to the trial believed that frenotomy would help their baby and that fewer than half were truly in equipoise, one of the commonest reported challenges by sites was low numbers of women willing to be randomised. One site reported that around 10 women had to be approached for everyone who expressed willingness to participate. While most women approached who did not wish to be randomised felt that frenotomy would benefit their baby and therefore were not willing to be randomised to a breastfeeding support only arm, there were a few women who strongly felt the opposite, that frenotomy was an unnecessary intervention and did not want their babies to have it. Other studies have reported that many parents feel that frenotomy is a beneficial intervention for breastfeeding difficulties and will go to considerable lengths to access the procedure;[35] however, analyses of online forum posts showed more variable experiences of its outcome.[36]

In many areas, capacity within infant feeding clinics and/or care pathways meant that women attended their first appointment only after they had been having difficulties with breastfeeding for some time. Only a third of babies recruited were <2 weeks old at trial entry (see *Table 1*). Many women felt that they had therefore already tried breastfeeding support without success, and therefore either were not willing to be randomised, or, if they were randomised to the breastfeeding support arm, they were willing only to try breastfeeding support alone for a few days before requesting frenotomy. Some sites gave women in the breastfeeding support arm 'just in case' appointments for frenotomy to address this concern, which had the effect of encouraging crossovers.

In the context of the COVID-19 pandemic, this was exacerbated, since parents were less willing to risk having to return for another clinic appointment and/or frenotomy when services were reduced, waiting times were longer and there were concerns over potential COVID-19 exposure by additional visits. Breastfeeding support services were known to be highly variable prior to the pandemic,[11] and this was exacerbated during the pandemic, with many services ceasing completely, or moving entirely online. Almost half of women completing the 2020 national maternity survey reported that they would have liked more support with breastfeeding compared to around 30% in the 2014 and 2018 surveys.[6]

Several sites had clinics that were named 'the frenotomy clinic' as opposed to the 'infant feeding clinic' or 'breastfeeding support service'. This naming meant that parents anticipated prior to arrival that their child would undergo frenotomy at the clinic, or shortly afterwards, which again contributed to a lack of equipoise. Some sites renamed their clinics to mitigate this barrier, which was felt to be making a difference to recruitment immediately prior to trial closure.

In some sites, assessment of tongue-tie and breastfeeding support advice was undertaken very early, on the postnatal ward prior to discharge. These sites felt that women were more in equipoise concerning whether or not frenotomy might be beneficial at this time, before they had been struggling with breastfeeding for days or weeks, and therefore that recruitment in the postnatal ward setting might be more effective.

Women in both arms had high rates of breastfeeding continuation, reflecting that they were a highly motivated population. Women recruited were more likely to live in more affluent areas and were older than the general population of women giving birth,[6] and almost all of those who had older children had breastfed before. All these factors are known to be associated with higher rates of breastfeeding[3] and may account for the high breastfeeding rates seen rather than any impact of the intervention.

It is of concern that women reported high levels of anxiety and depression both at recruitment, and, to a lesser extent, at 3 months, indicating an important need for mental health support.

Equality diversity and inclusion

The majority of women recruited to the trial were from White ethnic groups, despite the trial being conducted at sites with substantial ethnic minority populations. Six per cent of women recruited were from Asian or mixed ethnic backgrounds, and no participants recruited were from Black ethnic minority groups. It is unclear whether this reflects better community support for breastfeeding for women from Black and other ethnic minority groups, a lack of access to hospital breastfeeding support services or differential equipoise concerning frenotomy. Mothers from Black, mixed or other ethnic minority groups are more likely to breastfeed at 6 weeks.[5] Cultural traditions have been shown to be important in women's decisions about continuing breastfeeding[37] and there is a need for tailored support,[38] both of which may have influenced decisions to seek support from hospital infant feeding clinics and around the use of frenotomy.

Public and patient involvement

We included a PPI co-applicant from the Breastfeeding Network, who consulted with other Network members, and also established a Public Advisory Group. These two groups helped design the study processes and materials, and advised throughout the trial. We were also guided by a PPI member on the TSC. Patient and public involvement was challenged by the COVID-19 pandemic, and would have benefitted from greater diversity. At the time of trial closure we were planning further PPI work to determine whether there were areas of redesign that might help to address equipoise issues, but this was not carried out.

Implications for practice

The results of this trial provide no evidence of benefit of frenotomy with breastfeeding support over breastfeeding support given the small sample size. The high crossover rate indicates that the trial is at high risk of bias and cannot be used to guide practice. There is nevertheless some useful information to guide counselling of women with babies with tongue-tie. Babies in the breastfeeding support group with more restricted tongue movement, as measured using the BTAT, and whose mothers were in more pain, were more likely to undergo frenotomy. Mothers in both groups had high rates of breastfeeding continuation and reported less pain when feeding at 3 months, emphasising the importance of breastfeeding support to provide advice on latch and correct positioning. Complications of frenotomy were observed in about 1 in 50 babies.

Implications for research

The FROSTTIE trial has indicated that sufficient equipoise does not exist to conduct a randomised trial of frenotomy in NHS hospital infant feeding clinic settings. Such a trial may be possible if infants are recruited early, when initially consulting for breastfeeding support, ideally within community settings. However, it is likely that other study designs will need to be considered in the UK setting, for example observational studies alongside trials of other breastfeeding interventions such as the ABA-Feed study.[39]

Conclusions

This trial does not provide sufficient information to assess whether frenotomy in addition to breastfeeding support improves breastfeeding rates in infants diagnosed with tongue-tie. However, there were high breastfeeding rates in both arms. Complications of frenotomy were observed in about 1 in 50 infants. There is a clear lack of equipoise in the UK concerning the use of frenotomy, however, the effectiveness and cost-effectiveness of the procedure still need to be established. Other study designs will need to be considered to address this objective.

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Independent TSC

The trial was overseen by the Trial Steering Committee (TSC) who had ultimate responsibility for considering and, as appropriate, acting on the recommendations of the DMC. The TSC included an independent chair, four independent members, a PPI representative, a co-applicant and the Chief Investigator. Membership consisted of:

Professor Pat Hoddinott, Chair, Chair in Primary Care, NMAHP Research Unit, University of Stirling

Mr Mike Bradburn, Independent member, Senior Medical Statistician, University of Sheffield

Professor Debra Bick, Independent member, Professor of Clinical Trials in Maternal Health, Warwick Clinical Trials Unit, University of Warwick

Dr Mark Johnson, Independent member, Consultant Neonatologist, Department of Neonatal Medicine, University Hospital Southampton NHS Foundation Trust

Dr Sarah McMullen, Independent member (PPI member), Head of Knowledge, National Childbirth Trust

Dr Jenny Ingram, Independent member, Senior Research Fellow, Centre for Academic Child Health, University of Bristol

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Independent DMC

The Data Monitoring Committee (DMC), independent of the applicants and the TSC, reviewed the progress of the trial and interim analysis at least annually. They provided advice on the conduct of the trial to the TSC and (via the TSC) to the NIHR HTA programme.

Membership included the following:

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Ethics statement

The FROSTTIE trial protocol was approved by South Central – Oxford B Research Ethics Committee (ref. 18/SC/0580) on 10/12/2018 and the Health Research Authority (HRA) and may be found at https://www.npeu.ox.ac.uk/assets/downloads/frosttie/protocol/FROSTTIE_IRAS235355_clinical_research_protocol_v5_29Jul2020_clean_signed.pdf.

Local approval and site-specific assessments were obtained from each NHS hospital site.

Data-sharing statement

Data will be shared in accordance with the National Perinatal Epidemiology Unit Data Sharing policy. Requests for access to the data will be considered by the National Perinatal Epidemiology Unit Data Sharing committee. Access to anonymised data can be requested from general@npeu.ox.ac.uk or by contacting the corresponding author.

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Appendix 1 Participating units, principal investigators and site midwives

Recruiting sites for FROSTTIE	Principal Investigator(s)	Research Staff
Bradford Royal Infirmary	Sam Oddie	Jenny Eadle, Jennifer Syson
Cumberland Infirmary, Carlisle	John Elliott	Rachel Hardy
Darlington Memorial Hospital	Mehdi Garbash	Dawn Egginton, Jacqueline Jennings
George Eliot Hospital, Nuneaton	Olumuyiwa Olufemi Oso	Michelle Baxter, Alex Dunderdale, Jessica Gunn, Karen Shorthose, Tracy Truslove
Great Western Hospital, Swindon	Sarah Bates	KerryAnn Hanks, Kath Townsend
Homerton Hospital	Philippa Cox	Lisa Canclini, Angela Chiapparino, Rachel Frowd, Lisa Giacometti, Abigail Laurie
Leeds General Infirmary	Kathryn Johnson	Lindsay Uryn, Jackie Mullaney
Norfolk and Norwich University Hospital	Ashish Minocha	Louise Coke, Luisa Lyons
Queen Alexandra Hospital, Portsmouth	Zoe Garner	Andrew Gribbin, Hayley Nelson, Michelle Pople, Deirdre Rodgers, Amanda Tiller
Royal Albert and Edward Infirmary, Wigan	Steve Izzat	Kathryn Ashton, Claire Williams, Michelle Cooper, Jane Davies
Royal Berkshire Hospital, Reading	Fidelma Lee	Claire Carter
Royal Blackburn Hospital	Bev Hammond, Catharina Schram	Heather Collier, Gary Cousin, Laura Hindle, Louise Hoole, Jennifer McCallum, Matthew Milner, Maire Morton, Frances Pickering, Raheela Rafiq, Jeethendra Rao, Sam White
Royal Cornwall Hospital, Truro	Ruth Bowen	Barbara Bromage, Hannah Osborn
Royal United Hospital, Bath	Melody Rich	Catherine Bressington, Sara Burnard, Emma James, Annette Moreton, Jennifer Pullen, Sally Tedstone
Royal Victoria Infirmary, Newcastle	Paul Ayuk	Andrea Fenn, Lynne McDonald
Russells Hall Hospital, Dudley	Subramanian Mahadevan-Bava	Katy Penn, Lisa Williams
Stoke Mandeville Hospital, Aylesbury	Eliza Jones	Lisa Frankland, Julie Tebbutt, Danielle Thornton
Sunderland Royal Hospital	Lesley Hewitt	Judith Ormonde, Lucy Rowland
Worcestershire Royal Hospital	Catherine Townsend	Jessie Brain, Rebecca Davenport, Caroline Payne, Caroline Thunder, Hannah Wood

Note
Note that although 19 sites were opened, only 12 recruited participants.

Appendix 2 Sources of unit costs (UK British pounds 2017/18) used in the cost-analysis

TABLE 22 Categories of resource use and associated unit costs used in the analysis (expressed in 2019/20 UK pounds sterling)

Health-care resource use item	Unit cost	Source
Intervention-specific: Frenotomy		
Frenotomy with complications	£610	Frenotomy or Frenectomy Day Case (Code CA65Z). NHS Reference Costs 2019/2020 Version 2.
Frenotomy performed by doctor	£208	Weighted average of Frenotomy or Frenectomy Outpatient Procedures across service codes 217 (Paediatric Maxillo-Facial Surgery), 171 (Paediatric Surgery) and 420 (Paediatrics). NHS Reference Costs 2019/2020 Version 2.
Frenotomy performed by midwife and when the role of the person performing the procedure is missing	£103	Frenotomy or Frenectomy Outpatient Procedures, Midwifery Service (Service code 560). NHS Reference Costs 2019/2020 Version 2.
Frenotomy performed by other	£86	Weighted average of Frenotomy or Frenectomy Outpatient Procedures across service codes with the numbers of the procedures <100. NHS Reference Costs 2019/2020 Version 2.
Intervention-specific: breastfeeding support		
NHS, phone	£46	Health Visitor, Other Statutory Contact, Non-Face-to-Face [Code N03J, Community Health Services Health Visiting and Midwifery (HVM)]. NHS Reference Costs 2019/2020 Version 2.
NHS, in person	£81	Health Visitor, Other Statutory Contact, Face-to-Face [Code N03G, Community Health Services Health Visiting and Midwifery (HVM)]. NHS Reference Costs 2019/2020 Version 2.
Other, phone and in person	---	Assumed to be no expenses
Primary care		
General practitioner consultation	£39	Per typical 9.22 min consultation. Section 10.3b, Unit costs of Health and Social Care 2020.
General practitioner virtual consultation	£11	Average of GP face-to-face appointments and GP telephone calls. Section 10.4, Unit costs of Health and Social Care 2020.
Practice nurse consultation	£11	Per typical 15.5 minutes consultation (duration of consultation extracted from Unit Costs of Health and Social Care 2015). Section 10.2, Unit costs of Health and Social Care 2020.
Medications		
Course of promethazine hydrochloride assigned to mother`s prescription	£4.9	Cost of the pack is based on NHS drug tariff price for 25 mg tablets, size 56, one pack for the course. Electronic Drug Tariff March 2020.
Course of lamotrigine assigned to mother`s prescription	£17.3	Cost of the pack is based on NHS drug tariff price for 100 mg tablets (the most prescribed dosage based on Prescription Cost Analysis – England 2020/21), size 56, four packs for the course. Electronic Drug Tariff March 2020.

continued

TABLE 22 Categories of resource use and associated unit costs used in the analysis (expressed in 2019/20 UK pounds sterling) (*continued*)

Health-care resource use item	Unit cost	Source
Course of citalopram assigned to mother's prescription	£2.7	Cost of the pack is based on NHS drug tariff price for 20 mg tablets (the most prescribed dosage based on Prescription Cost Analysis – England 2020/21), size 28, three packs for the course. Electronic Drug Tariff March 2020.
Course of fluoxetine assigned to mother's prescription	£2.0	Cost of the pack is based on NHS drug tariff price for 20 mg capsules (the most prescribed dosage based on Prescription Cost Analysis – England 2020/21), size 30, two packs for the course. Electronic Drug Tariff March 2020.
Course of sertraline assigned to mother's prescription	£2.5	Cost of the pack is based on NHS drug tariff price for 50 mg tablets (the most prescribed dosage based on Prescription Cost Analysis – England 2020/21), size 28, two packs for the course. Electronic Drug Tariff March 2020.
Course of flucloxacillin assigned to mother's prescriptions for ductal infection and mastitis in lactating women	£5.4	Cost of the pack is based on NHS drug tariff price for 500 mg capsules (the most prescribed dosage based on Prescription Cost Analysis – England 2020/21), size 28, two packs for the course. Electronic Drug Tariff March 2020.
Course of co-amoxiclav assigned to mother's prescriptions for C-section wound infection	£2.5	Cost of the pack is based on NHS drug tariff price for 500 mg/125 mg tablets (the most suitable dosage based on single dose), size 21, one pack for the course. Electronic Drug Tariff March 2020.
Course of amoxicillin assigned to mother's prescriptions for pericoronitis and acute bronchitis	£1.1	Cost of the pack is based on NHS drug tariff price for 500 mg capsules (the most prescribed dosage based on Prescription Cost Analysis – England 2020/21), size 15, one pack for the course. Electronic Drug Tariff March 2020.
Course of trimethoprim assigned to mother's prescriptions for low urinary tract infection	£0.4	Cost of the pack is based on NHS drug tariff price for 200 mg tablets (the most prescribed dosage based on Prescription Cost Analysis – England 2020/21), size 6, one pack for the course. Electronic Drug Tariff March 2020.
Course of cefalexin assigned to mother's prescriptions for sepsis	£2.2	Cost of the pack is based on NHS drug tariff price for 500 mg capsules (the most prescribed dosage based on Prescription Cost Analysis – England 2020/21), size 21, one pack for the course. Electronic Drug Tariff March 2020.
Course of fluconazole assigned to mother's prescriptions for candida – female genital	£0.9	Cost of the pack is based on NHS drug tariff price for 150 mg capsules (the most prescribed dosage based on Prescription Cost Analysis – England 2020/21), size 1, one pack for the course. Electronic Drug Tariff March 2020.
Course of gentamicin with hydrocortisone assigned to mother's prescriptions for acute otitis externa	£33.3	Cost of the pack is based on NHS drug tariff price for Gentamicin 0.3%/Hydrocortisone acetate 1% ear drops, 10 ml, one pack for the course. Electronic Drug Tariff March 2020.
Course of amoxicillin assigned to infant's prescriptions for suspected throat infection and stomach infection	£3.2	Cost of the bottle is based on NHS drug tariff price for 125 mg/5 ml oral suspension, 100 ml, one bottle for the course. Electronic Drug Tariff March 2020.
Course of nystatin assigned to infant's prescriptions for oral candidiasis	£2.7	Cost of the pack is based on NHS drug tariff price for 100,000 units/ml oral suspension, 30 ml, one pack for the course. Electronic Drug Tariff March 2020.
Course of chloramphenicol assigned to infant's prescriptions for conjunctivitis	£4.0	Cost of the pack is based on NHS drug tariff price for 0.5% drops, 10 ml, one pack for the course. Electronic Drug Tariff March 2020.
Course of flucloxacillin assigned to infant's prescriptions for infected eczema and fungal skin infection	£5.7	Cost of the bottle is based on NHS drug tariff price for 125 mg/5 ml oral suspension, 100 ml, two bottles for the course. Electronic Drug Tariff March 2020.

TABLE 22 Categories of resource use and associated unit costs used in the analysis (expressed in 2019/20 UK pounds sterling) (*continued*)

Health-care resource use item	Unit cost	Source
Course of trimethoprim assigned to infant's prescriptions for vesicoureteral Reflux (VUR)	£5.0	Cost of the bottle is based on NHS drug tariff price for 50 mg/5 ml oral suspension sugar free, 100 ml, one bottle for the course. Electronic Drug Tariff March 2020.
Course of amoxicillin assigned to infant's prescriptions for bacterial infection	£6.4	Cost of the bottle is based on NHS drug tariff price for 125 mg/5 ml oral suspension, 100 ml, two bottles for the course. Electronic Drug Tariff March 2020.
Course of cefalexin assigned to infant's prescriptions for urinary infection	£2.0	Cost of the bottle is based on NHS drug tariff price for 125 mg/5 ml oral suspension, 100 ml, one bottle for the course. Electronic Drug Tariff March 2020.
Community care		
Community nurse/midwife contact, virtual		
Mother	£27	Weighted average of Community Health Services Non-Face-to-Face Nursing (NURS) N02AN and N29AN codes. NHS Reference Costs 2019/2020 Version 2.
Community nurse/midwife contact, in person		
Mother	£47	Weighted average of Community Health Services Health Visiting and Midwifery (HVM) N01P code and Face-to-Face Nursing (NURS) N09AF and N29AF codes. NHS Reference Costs 2019/2020 Version 2.
Infant	£84	Weighted average of Community Health Services Health Visiting and Midwifery (HVM) N01P code and Face-to-Face Nursing (NURS) N29CF code. NHS Reference Costs 2019/2020 Version 2.
Infant Health visitor contact, virtual	£46	Health Visitor, Other Statutory Contact, Non Face-to-Face [Code N03J, Community Health Services Health Visiting and Midwifery (HVM)]. NHS Reference Costs 2019/2020 Version 2.
Infant Health visitor contact, in person	£81	Health Visitor, Other Statutory Contact, Face-to-Face [Code N03G, Community Health Services Health Visiting and Midwifery (HVM)]. NHS Reference Costs 2019/2020 Version 2.
Community paediatrician visit	£350	Weighted average of consultant and non-consultant Face-to-Face Community Paediatrics Outpatient Attendance (Service Code 290) WF01A and WF01B codes. NHS Reference Costs 2019/2020 Version 2.
Secondary (hospital-based) care		
Accident & Emergency department visit, mother or infant	£182	Weighted average of all Emergency Medicine contact codes excluding cases dead on arrival. NHS Reference Costs 2019/2020 Version 2.
Hospital outpatient clinic appointment, virtual		
Mother	£72	Weighted average of Non-Face-to-Face General Medicine and General Surgery Outpatient Attendance (Service Codes 300 and 100) WF01C, WF01D, WF02C, WF02D codes. NHS Reference Costs 2019/2020 Version 2.
Hospital outpatient clinic appointment, in person		
Mother	£165	Weighted average of Face-to-Face General Medicine and General Surgery Outpatient Attendance (Service Codes 300 and 100) WF01A, WF01B, WF02A, WF02B codes. NHS Reference Costs 2019/2020 Version 2.

continued

TABLE 22 Categories of resource use and associated unit costs used in the analysis (expressed in 2019/20 UK pounds sterling) (*continued*)

Health-care resource use item	Unit cost	Source
Infant	£231	Weighted average of Face-to-Face Paediatrics, Paediatric Surgery and Neonatology Outpatient Attendance (Service Codes 420, 171 and 422) WF01A, WF01B, WF02A, WF02B codes. NHS Reference Costs 2019/2020 Version 2.
Hospital admission due to mother's sepsis	£668	Weighted average of Non-elective Short Stay hospital admissions across codes WJ06A, WJ06B, WJ06C, WJ06D, WJ06E, WJ06F, WJ06G, WJ06H, WJ06J (Sepsis). NHS Reference Costs 2019/2020 Version 2.
Hospital admission due to mother's infusion of rituximab	£1548	Sum of Follow-up Examination for Other Conditions, with Interventions, Day case admissions, code WH53A and national average unit cost of rituximab, high cost drugs, code PHCD00089. NHS Reference Costs 2019/2020 Version 2.
Hospital admissions due to infant's stomach infection and clostridium difficile	£540	Weighted average of Non-elective Short Stay hospital admissions across codes PF21A and PF21B (Paediatric, Infectious or Non-Infectious Gastroenteritis). NHS Reference Costs 2019/2020 Version 2.
Hospital admissions due to infant's prolonged jaundice	£517	Weighted average of Non-elective Short Stay hospital admissions across codes GC18A and GC18B (Non-Obstructive Jaundice). NHS Reference Costs 2019/2020 Version 2.
Hospital admissions due to infant's bronchiolitis	£612	Weighted average of Non-elective Short Stay hospital admissions across codes PD15A, PD15B, PD15C, PD15D (Paediatric Acute Bronchiolitis). NHS Reference Costs 2019/2020 Version 2.
Hospital admissions due to infant's poor weight gain or weight loss	£558	Weighted average of Non-elective Short Stay hospital admissions across codes PX57A, PX57B, PX57C (Paediatric, Examination, Follow-up, Special Screening or Other Admissions). NHS Reference Costs 2019/2020 Version 2.
Hospital admissions due to infant's high temperature	£543	Weighted average of Non-elective Short Stay hospital admissions across codes PW20A, PW20B, PW20C (Paediatric Fever of Unknown Origin). NHS Reference Costs 2019/2020 Version 2.
Hospital admissions due to infant's breathing issues	£651	Weighted average of Non-elective Short Stay hospital admissions across codes PD12A, PD12B, PD12C (Paediatric, Asthma or Wheezing). NHS Reference Costs 2019/2020 Version 2.
Hospital admissions due to infant's accidental injury	£622	Weighted average of Non-elective Short Stay hospital admissions across codes PV08A, PV08B, PV31A, PV31B, PV32A, PV32B, PV32C (Paediatric Minor Injury without Intracranial Injury, Paediatric Intermediate Injury without Intracranial Injury, Paediatric Major Injury without Intracranial Injury). NHS Reference Costs 2019/2020 Version 2.
Hospital admissions due to infant's suspected sepsis	£574	Sepsis without Interventions, with CC Score 0-4, Non-elective Short Stay hospital admissions, code WJ06J. NHS Reference Costs 2019/2020 Version 2.
Hospital admissions due to infant's urinary tract infections	£593	Weighted average of Non-elective Short Stay hospital admissions across codes PW01A, PW01B, PW01C, PW16A, PW16B, PW16C, PW16D, PW16E, PW17D, PW17E, PW17F, PW17G (Paediatric Minor Infections, Paediatric Intermediate Infections, Paediatric Major Infections). NHS Reference Costs 2019/2020 Version 2.
Other health-care professional contacts		
Health visitor visits, mother	£81	Health Visitor, Other Statutory Contact, Face-to-Face [Code N03G, Community Health Services Health Visiting and Midwifery (HVM)]. NHS Reference Costs 2019/2020 Version 2.

TABLE 22 Categories of resource use and associated unit costs used in the analysis (expressed in 2019/20 UK pounds sterling) (*continued*)

Health-care resource use item	Unit cost	Source
Neurologist visits, mother	£220	Weighted average of consultant and non-consultant led Face-to-Face Neurology Outpatient Attendance (Service Code 400) across codes WF01A and WF01B. NHS Reference Costs 2019/2020 Version 2.
Physiotherapist contacts, mother	£42	Weighted average of consultant and non-consultant led Non-Face-to-Face Physiotherapy Outpatient Attendance (Service Code 650) across codes WF01C and WF01D. NHS Reference Costs 2019/2020 Version 2.
Physiotherapist visits, mother	£64	Weighted average of consultant and non-consultant led Face-to-Face Physiotherapy Outpatient Attendance (Service Code 650) across codes WF01A, WF01B and Physiotherapist, Adult, One to One code A08A1 (Community Health Services, service code AHP). NHS Reference Costs 2019/2020 Version 2.
Physiotherapist visits, infant	£68	Weighted average of consultant and non-consultant led Face-to-Face Physiotherapy Outpatient Attendance (Service Code 650) across codes WF01A, WF01B and Physiotherapist, Child, One to One code A08C1 (Community Health Services, service code AHP). NHS Reference Costs 2019/2020 Version 2.
Therapist contacts, mother	£337	Weighted average of consultant and non-consultant led Non-Face-to-Face Adult Mental Illness (Service Code 710) across codes WF01C, WF01D. NHS Reference Costs 2019/2020 Version 2.
Perinatal psychiatrist visits, mother	£223	Weighted average of Community Contacts (code SPHMSMBUCC) and Outpatient Attendances (code SPHMSMBUOP) Specialist Perinatal Mental Health Services, Mental Health, service code SPMHS. NHS Reference Costs 2019/2020 Version 2.
Dietitian contacts, mother	£92	Dietitian (code A03), Allied Health Professionals (service code AHP), Community Health Services. NHS Reference Costs 2019/2020 Version 2.
Ophthalmologists visits, mother	£108	Weighted average of consultant and non-consultant led Face-to-Face Outpatient Attendances (Ophthalmology, Service Code 130) across codes WF01A, WF01B. NHS Reference Costs 2019/2020 Version 2.
Gynaecologist visits, mother	£157	Weighted average of consultant and non-consultant led Face-to-Face Outpatient Attendances (Gynaecology, Service Code 502) across codes WF01A, WF01B. NHS Reference Costs 2019/2020 Version 2.
Allergy paediatrician visits	£255	Weighted average of consultant and non-consultant led Face-to-Face Outpatient Attendances (Paediatric Clinical Immunology and Allergy Service, Service Code 255) across codes WF01A, WF01B. NHS Reference Costs 2019/2020 Version 2.
Consultant orthopaedic nurse visits	£144	Weighted average of consultant led Face-to-Face Outpatient Attendances (Paediatric Trauma and Orthopaedics, Service Code 214) across codes WF01A, WF01B. NHS Reference Costs 2019/2020 Version 2.
Paediatric surgeon visits	£172	Weighted average of consultant and non-consultant led Face-to-Face Outpatient Attendances (Paediatric Surgery, Service Code 171) across codes WF01A, WF01B. NHS Reference Costs 2019/2020 Version 2.
Sonographer visits	£54	Weighted average of Consultant Led, Non Consultant Led and Outpatient Procedures Ultrasound (non-obstetric) (code DIM007). NHS Reference Costs 2019/2020 Version 2.
Radiographer visits	£58	Weighted average of Consultant Led, Non Consultant Led and Outpatient Procedures Ultrasound (non-obstetric) (code DIM007). NHS Reference Costs 2019/2020 Version 2.
Ostheopath visits	£47	Assumed to be out of pocket expenses. The average cost of £47 as a unit cost for the osteopath session is based on £40 to £55 for a 30- to 40-minute session. https://www.nhs.uk/conditions/osteopathy/

TABLE 23 Total number of frenotomies performed for the whole study cohort from trial entry up to 3 months after birth

	Total (*n* = 169), *n* (%)
Frenotomies performed by a private provider	**0**
Frenotomies performed by the NHS provider	**140 (82.8)**
Doctor	19 (11.2)
Midwife	117 (69.2)
Other	1 (0.6)
Missing	3 (1.8)
Frenotomies with complications	3 (1.8)
Frenotomies not performed	**29 (17.2)**

TABLE 24 Breastfeeding support received in the 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across women who received breastfeeding support

	Frenotomy with breastfeeding support (*n* = 80)		Breastfeeding support only (*n* = 89)		
	Number of patients (%)	Mean number of contacts (SD)	Number of patients (%)	Mean number of contacts (SD)	Mean difference in number of contacts (95% CI)*
Total breast-feeding support received	**50 (62.5)**	**3.64 (2.8)**	**60 (67.4)**	**3.32 (2.57)**	**0.2 (−0.81 to 1.21)**
NHS contacts	43 (53.75)	2.72 (1.65)	49 (55.0)	3.16 (2.4)	−0.31 (−1.2 to 0.57)
Phone	26 (60.5)	2 (0.98)	32 (65.3)	1.72 (1.37)	
In person	29 (67.4)	2.24 (1.64)	37 (75.5)	2.7 (2.28)	
Missing	8 (10.0)	---	14 (15.73)	---	
Other contacts	18 (22.5)	3.61 (2.7)	15 (16.85)	2.93 (2.05)	0.93 (−1.21 to 3.08)
Phone	9 (50.0)	3.11 (1.96)	12 (75.0)	2.33 (1.92)	
In person	14 (77.8)	2.64 (1.82)	10 (62.5)	1.6 (1.35)	
Missing	8 (10.0)	---	15 (16.58)	---	
Not received	22 (27.5)	---	14 (15.73)	---	

TABLE 25 Maternal health-care resource use by category and item between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across women who consumed the resource use

Resource use category and item	Frenotomy with breastfeeding support (*n* = 80)		Breastfeeding support only (*n* = 89)		
	Number of patients (%)	Mean number of contacts* (SD)	Number of patients (%)	Mean number of contacts (SD)†	Mean difference in number of contacts (95% CI)†
Primary care					
General practitioner visits	42 (52.5)	1.59 (0.91)	32 (36.0)	1.47 (0.91)	0.07 (−0.39 to 0.53)
Missing	7 (8.75)	---	16 (17.98)	---	
Practice nurse visits	3 (3.75)	4 (3)	4 (4.5)	2 (0.82)	2.81 (−37.36 to 42.98)
Missing	7 (8.75)	---	15 (16.85)	---	
Medicines, of which	14 (17.5)	1.5 (0.94)	7 (7.9)	1.57 (0.79)	0.16 (−0.86 to 1.19)
Antibiotics	13 (16.25)	1.38 (0.65)	6 (6.7)	1.5 (0.84)	
For anxiety/ depression	2 (2.5)	1.5 (0.7)	2 (2.2)	1 (0)	
Missing	7 (8.75)	---	15 (16.85)	---	
Community care					
Community nurse/ midwife contacts, of which	3 (3.75)	1.67 (0.58)	2 (2.25)	1.5 (0.71)	Not possible to calculate
Virtual	0	-	1 (1.1)	1(-)	
In person	3 (3.75)	1.67 (0.58)	2 (2.25)	1 (0)	
Missing	7 (8.75)	---	15 (16.85)	---	
Secondary (hospital-based) care					
Accident & emergency department visits	1 (1.25)	2 (-)	1 (1.1)	1 (-)	Not possible to calculate
Missing	7 (8.75)	---	15 (16.85)	---	
Hospital outpatient clinic appointments, of which	6 (7.5)	1.67 (0.82)	2 (2.25)	2 (1.41)	−0.25 (−1.89 to 1.4)
Virtual	1 (1.25)	2 (-)	0	-	
In person	6 (7.5)	1.33 (0.52)	2 (2.25)	2 (1.41)	
Missing	7 (8.75)	---	15 (16.85)	---	
Hospital admissions	1 (1.25)	1 (-)	1 (1.1)	1 (-)	Not possible to calculate
Length of stay (days)		1 (-)		2 (-)	Not possible to calculate
Missing	8 (10.0)	---	14 (15.7)	---	

continued

TABLE 25 Maternal health-care resource use by category and item between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across women who consumed the resource use (*continued*)

Resource use category and item	Frenotomy with breastfeeding support (*n* = 80)		Breastfeeding support only (*n* = 89)		Mean difference in number of contacts (95% CI)[b]
	Number of patients (%)	Mean number of contacts* (SD)	Number of patients (%)	Mean number of contacts (SD)[a]	
Any other NHS health-care professionals contacts					
Other NHS health-care professional contacts, of which	7 (8.75)	2 (0.82)	5 (5.6)	2.4 (1.14)	−0.84 (−2.51 to 0.83)
Virtual	2 (2.5)	2 (0)	2 (2.25)	3.5 (0.71)	
In person	7 (8.75)	1.43 (0.53)	3 (3.3)	1.67 (0.58)	
Missing	7 (8.75)	---	15 (16.85)	---	
Any other non-NHS health-care professional contacts					
Osteopath visits	0	-	2 (2.2)	2.5 (0.71)	Not possible to calculate
Missing	7 (8.75)	---	15 (16.85)	---	

a Mean number of courses received in the medicines and mean number of hospital admissions in the hospital admissions.
b Adjusted for centre, infant's age at randomisation and parity.

TABLE 26 Infants' health-care resource use by category and item between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across infants who consumed the resource use

Resource use category and item	Frenotomy with breastfeeding support (*n* = 80)		Breastfeeding support only (*n* = 89)		Mean difference in number of contacts (95% CI)[b]
	Number of patients (%)	Mean number of contacts (SD)[a]	Number of patients (%)	Mean number of contacts (SD)[a]	
Primary care					
General practitioner contacts, of which	42 (52.5)	1.5 (0.71)	37 (41.57)	1.68 (1.03)	−0.18 (−0.59 to 0.23)
Virtual	0	-	1 (1.1)	1 (-)	
In person	42 (52.5)	1.5 (0.71)	37 (41.6)	1.65 (1.01)	
Missing	7 (8.75)	---	17 (19.10)	---	
Practice nurse visits	5 (6.25)	1.8 (0.45)	6 (6.75)	1.67 (0.52)	0.11 (−1.24 to 1.45)
Missing	7 (8.75)	---	15 (16.85)	---	
Medicines (antibiotics)	4 (5.0)	1 (0)	6 (6.75)	1 (0)	
Missing	7 (8.75)	---	15 (16.85)	---	

TABLE 26 Infants' health-care resource use by category and item between 'Frenotomy with breastfeeding support' and 'Breastfeeding support only' groups from trial entry up to 3 months after birth across infants who consumed the resource use (*continued*)

Resource use category and item	Frenotomy with breastfeeding support (*n* = 80)		Breastfeeding support only (*n* = 89)		Mean difference in number of contacts (95% CI)[b]
	Number of patients (%)	Mean number of contacts (SD)[a]	Number of patients (%)	Mean number of contacts (SD)[a]	
Community care					
Community nurse/ midwife visits	1 (1.25)	8 (-)	2 (2.2)	1 (0)	Not possible to calculate
Missing	7 (8.75)	---	15 (16.85)	---	
Infant health visitor contacts, of which	5 (6.25)	3.6 (1.67)	7 (7.9)	2.0 (1.0)	2.4 (−0.82 to 5.56)
Virtual	1 (1.25)	6 (-)	1 (1.1)	1 (-)	
In person	4 (5.0)	3 (1.15)	7 (7.9)	1.86 (1.07)	
Missing	8 (10.0)	---	15 (16.85)	---	
Community paediatrician visits	1 (1.25)	1 (-)	2 (2.2)	1 (0)	Not possible to calculate
Missing	7 (8.75)	---	15 (16.85)	---	
Secondary (hospital-based) care					
Accident & emergency department visits	4 (5.0)	1.25 (0.5)	3 (3.4)	1 (0)	Not possible to calculate
Missing	7 (8.75)	---	15 (16.85)	---	
Hospital outpatient clinic appointments	5 (6.25)	2.4 (3.13)	2 (2.2)	1.5 (0.71)	5.3 (−45.62 to 56.24)
Missing	7 (8.75)	---	15 (16.85)	---	
Hospital admissions	4 (5.0)	1.75 (1.5)	9 (10.1)	1.11 (0.33)	0.5 (−1.74 to 2.74)
Length of stay (days)		6 (8)		2 (1)	4 (−7 to 15)
Missing	8 (10.0)	---	14 (15.7)	---	
Any other NHS health-care professional visits					
Other NHS health-care professional visits	2 (2.5)	2 (1.41)	2 (2.2)	1.5 (0.71)	Not possible to calculate
Missing	8 (10.0)	---	17 (19.1)	---	
Any other non-NHS health-care professional visits					
Osteopath visits	2 (2.5)	1.5 (0.71)	4 (4.5)	2.0 (0.82)	−1.03 (−7.45 to 5.4)
Missing	8 (10.0)	---	17 (19.1)	---	

a Mean number of courses received in the medicines and mean number of hospital admissions in the hospital admissions.
b Adjusted for centre, infant's age at randomisation and parity.

TABLE 27 Maternal and infant cost analysis across all participants involved in the trial (expressed in 2019/20 UK pounds sterling)

Resource use category and item	Total (*n* = 169), mean cost (SD)	
	Mother	Infant
Frenotomy [1]		**£106 (£87)**
Missing, n (%)		---
Breastfeeding support		
NHS contacts, phone	£33 (£54)	
NHS contacts, in person	£91 (£149)	
Total NHS contacts breastfeeding support [2]	**£124 (£158)**	
Missing, n (%)	22 (13.0)	
Primary care		
General practitioner visits	£30 (£39)	£33 (£39)
Missing, n (%)	23 (13.6)	24 (14.2)
Practice nurse visits	£1.5 (£8.2)	£1.4 (£5.2)
Missing, n (%)	22 (13.0)	22 (13.0)
Primary care, total	£32 (£41)	£35 (£40)
Missing, n (%)	24 (14.2)	25 (14.8)
Primary care, total mother/infant pair [3]	**£67 (£66)**	
Missing, n (%)	25 (14.8)	
Medicines		
Antibiotics	£1.1 (£5.8)	£0.3 (£1.1)
For anxiety/depression	£0.2 (£1.7)	---
Medicines, total	£1.3 (£7.4)	£0.3 (£1.1)
Missing, n (%)	22 (13.0)	22 (13.0)
Medicines, total mother/infant pair [4]	**£1.6 (£7.5)**	
Missing, n (%)	22 (13.0)	
Community care		
Community nurse/midwife contacts	£2 (£13)	£6 (£56)
Missing, n (%)	22 (13.0)	22 (13.0)
Infant Health Visitor contacts	---	£16 (£59)
Missing, n (%)	---	23 (13.6)
Community Paediatrician visits	---	£7 (£50)
Missing, n (%)	---	22 (13.0)
Community care, total	£2 (£13)	£27 (£99)
Missing, n (%)	22 (13.0)	23 (13.6)
Community care, total mother/infant pair [5]	**£29 (£99)**	
Missing, n (%)	23 (13.6)	
Secondary (hospital-based) care		
Accident & emergency department visits	£4 (£33)	£10 (£47)
Missing, n (%)	22 (13.0)	22 (13.0)

TABLE 27 Maternal and infant cost analysis across all participants involved in the trial (expressed in 2019/20 UK pounds sterling) (*continued*)

Resource use category and item	Total (*n* = 169), mean cost (SD)	
	Mother	Infant
Hospital outpatient clinic appointments	£14 (£66)	£24 (£162)
Missing, n (%)	22 (13.0)	22 (13.0)
Hospital admissions	£15 (£139)	£67 (£258)
Missing, n (%)	22 (13.0)	22 (13.0)
Secondary (hospital-based) care, total	£33 (£158)	£101 (£418)
Missing, n (%)	23 (13.6)	23 (13.6)
Secondary (hospital-based) care, total mother/infant pair [6]	**£135 (£451)**	
Missing, n (%)	23 (13.6)	
Any other NHS health-care professional contacts		
Other NHS health-care professional contacts, total	£22 (£121)	£5 (£36)
Missing, n (%)	22 (13.0)	22 (13.0)
Other NHS health-care professional contacts, total mother/infant pair [7]	**£27 (£130)**	
Missing, n (%)	22 (13.0)	
Any other non-NHS health-care costs		
Payment for anything to help breastfeeding	£7 (£26)	---
Missing, n (%)	31 (18.0)	
Non-NHS health-care professional visits, osteopath	£2 (£14)	£4 (£18)
Missing, n (%)	22 (13.0)	25 (15.0)
Other non-NHS health-care costs, total mother/infant pair [8]	**£7 (£26)**	
Missing, n (%)	34 (20.0)	
Total maternal/infant costs [1] + [2] + [3] + [4] + [5] + [6] + [7]	**£217 (£293)**	**£274 (£580)**
Missing, n (%)	26 (15.4)	27 (16.0)
Total cost mother/infant pair [1] + [2] + [3] + [4] + [5] + [6] + [7]	**£490 (£707)**	
Missing, n (%)	28 (16.6)	

TABLE 28 Distribution of EQ-5D-5L responses across the dimensions at different follow-up periods

Follow-up point	Mobility		Self-care		Usual activities		Pain/discomfort		Anxiety/depression	
	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)
Baseline (trial entry)										
No problems	57 (74)	66 (76)	65 (83)	77 (88.5)	50 (64.1)	50 (58.1)	23 (29.5)	24 (28)	49 (62.8)	47 (54)
Slight problems	15 (19.5)	17 (19.5)	12 (15.5)	8 (9.2)	18 (23.1)	21 (24.4)	36 (46)	38 (44)	16 (20.5)	27 (31)
Moderate problems	5 (6.5)	4 (4.5)	1 (1.5)	2 (2.3)	9 (11.5)	12 (14)	17 (22)	18 (21)	10 (12.8)	11 (12.7)
Severe problems	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (2.3)	2 (2.5)	6 (7)	3 (3.9)	2 (2.3)
Unable to	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.3)	1 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)
Total	77 (100)	87 (100)	78 (100)	87 (100)	78 (100)	86 (100)	78 (100)	86 (100)	78 (100)	87 (100)
χ^2 (*p*-value)	0.2860	0.867	1.6615	0.436	2.2745	0.685	1.7177	0.633	2.6201	0.454
Missing	3 (3.7)	2 (2.3)	2 (2.5)	2 (2.3)	2 (2.5)	3 (3.4)	2 (2.5)	3 (3.4)	2 (2.5)	2 (2.3)
Routine follow-up (approximately one to 2 weeks post-trial entry)										
No problems	66 (85.7)	66 (76)	70 (90.9)	75 (86.2)	54 (70)	61 (70)	42 (55.3)	41 (47)	360 (50)	58 (66.7)
Slight problems	7 (9.1)	21 (24)	5 (6.5)	11 (12.6)	16 (20.8)	19 (21.8)	28 (36.8)	39 (45)	313 (44)	25 (28.7)
Moderate problems	4 (5.2)	0 (0)	2 (2.6)	1 (1.2)	6 (7.8)	6 (7)	5 (6.5)	7 (8)	44 (6)	2 (2.3)
Severe problems	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.4)	1 (1.2)	1 (1.3)	0 (0)	0 (0)	2 (2.3)

TABLE 28 Distribution of EQ-5D-5L responses across the dimensions at different follow-up periods (*continued*)

	Mobility		Self-care		Usual activities		Pain/discomfort		Anxiety/depression	
Follow-up point	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)	Frenotomy w/ breastfeeding support (*n* = 80)	Breastfeeding support (*n* = 89)
Unable to	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total	77 (100)	87 (100)	77 (100)	87 (100)	77 (100)	87 (100)	76 (100)	87 (100)	77 (100)	87 (100)
χ^2 (*p*-value)	**10.429**	**0.005**	2.154	0.341	0.0737	0.995	2.42	0.49	5.0758	0.166
Missing	3 (3.7)	2 (2.3)	3 (3.7)	2 (2.3)	3 (3.7)	2 (2.3)	4 (5)	2 (2.3)	3 (3.7)	2 (2.3)
3 months after birth										
No problems	63 (86.3)	68 (90.3)	66 (90.5)	71 (95)	59 (80.8)	62 (82.7)	46 (63)	48 (64)	44 (60.3)	49 (65)
Slight problems	6 (8.3)	6 (8)	5 (6.8)	4 (5)	10 (13.7)	8 (10.7)	20 (27.4)	22 (29)	22 (30)	18 (24)
Moderate problems	2 (2.7)	1 (1.3)	2 (2.7)	0 (0)	3 (4.1)	5 (6.7)	4 (5.5)	3 (4)	5 (7)	8 (11)
Severe problems	2 (2.7)	0 (0)	0 (0)	0 (0)	1 (1.4)	0 (0)	3 (4.1)	2 (3)	2 (2.7)	0 (0)
Unable to walk	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total	73 (100)	75 (100)	73 (100)	75 (100)	73 (100)	75 (100)	73 (100)	75 (100)	73 (100)	75 (100)
χ^2 (*p*-value)	2.4976	0.476	2.267	0.322	1.7699	0.622	0.4537	0.929	3.3347	0.343
Missing	7 (8.7)	14 (15.7)	7 (8.7)	14 (15.7)	7 (8.7)	14 (15.7)	7 (8.7)	14 (15.7)	7 (8.7)	14 (15.7)

Note
Bold figures indicate significant differences at 5% level; unable to refers to extreme pain/discomfort in that domain; unable to refers to extremely anxious/depression in that domain.

Appendix 3 Summary of changes to the study protocol

Amendment no.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made
N/A	1	27/09/18		Initial version submitted to REC.
N/A	2	06/12/18	Changes made on behalf of PMG	Amendments made in accordance with NIHR (funder) and REC recommendations. Additional minor corrections to ensure consistency throughout.
N/A	3	25/03/19	Changes made on behalf of PMG	Amendments made to exclusion criteria and SAE reporting; and minor corrections to wording in sections 3, 7 and 10.
N/A	4	28/06/19	Changes made on behalf of PMG	Masking removed from study design as per NIHR (funder) request. Adverse event data collection updated. Minor clarification to number of recruiting centres needed. Authorship criteria clarified. Minor changes to grammar for clarification.
N/A	5	28/07/2020	Changes made on behalf of PMG	Virtual assessments and breastfeeding support, and virtual BTAT assessment permitted within trial. Verbal consent permitted if written consent is not possible. COVID-19 status of mother and baby collected. Minor corrections to references.

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