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Avoidance of bottles during the establishment of breast feeds in preterm infants (Review)

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[Intervention Review]

Avoidance of bottles during the establishment of breast feeds in preterm infants

Carmel T Collins[1], Jennifer Gillis[2], Andrew J McPhee[3], Hiroki Suganuma[4], Maria Makrides[5]

[1]Healthy Mothers, Babies and Children, South Australian Health and Medical Research Institute, North Adelaide, Australia. [2]Special Care Baby Unit, Women's and Children's Hospital, North Adelaide, Australia. [3]Neonatal Medicine, Women's and Children's Hospital, North Adelaide, Australia. [4]Department of Pediatrics, Juntendo University School of Medicine, Tokyo, Japan. [5]Healthy Mothers, Babies and Children, South Australian Health and Medical Research Institute, Adelaide, Australia

Contact address: Carmel T Collins, Healthy Mothers, Babies and Children, South Australian Health and Medical Research Institute, 72 King William Road, North Adelaide, South Australia, 5006, Australia. carmel.collins@sahmri.com.

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ABSTRACT

Background

Preterm infants start milk feeds by gavage tube. As they mature, sucking feeds are gradually introduced. Women who choose to breast feed their preterm infant are not always able to be in hospital with their baby and need an alternative approach to feeding. Most commonly, milk (expressed breast milk or formula) is given by bottle. Whether using bottles during establishment of breast feeds is detrimental to breast feeding success is a topic of ongoing debate.

Objectives

To identify the effects of avoidance of bottle feeds during establishment of breast feeding on the likelihood of successful breast feeding, and to assess the safety of alternatives to bottle feeds.

Search methods

We used the standard search strategy of the Cochrane Neonatal Review Group to search the Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 2), MEDLINE via PubMed (1966 to July 2016), Embase (1980 to July 2016) and CINAHL (1982 to July 2016). We also searched databases of clinical trials and the reference lists of retrieved articles for randomised controlled trials and quasi-randomised trials.

Selection criteria

Randomised and quasi-randomised controlled trials comparing avoidance of bottles with use of bottles in women who have chosen to breast feed their preterm infant.

Data collection and analysis

Two review authors independently assessed trial quality and extracted data. When appropriate, we contacted study authors for additional information. Review authors used standard methods of The Cochrane Collaboration and the Cochrane Neonatal Review Group.

Main results

We included seven trials with 1152 preterm infants. Five studies used a cup feeding strategy, one used a tube feeding strategy and one used a novel teat when supplements to breast feeds were needed. We included the novel teat study in this review, as the teat was designed to more closely mimic the sucking action of breast feeding. The trials were of small to moderate size, and two had high risk of attrition

bias. Adherence with cup feeding was poor in one of the studies, indicating dissatisfaction with this method by staff and/or parents; the remaining four cup feeding studies provided no such reports of dissatisfaction or low adherence. Meta-analyses provided evidence of low to moderate quality indicating that avoiding bottles increases the extent of breast feeding on discharge home (full breast feeding typical risk ratio (RR) 1.47, 95% confidence interval (CI) 1.19 to 1.80; any breast feeding RR 1.11, 95% CI 1.06 to 1.16). Limited available evidence for three months and six months post discharge shows that avoiding bottles increases the occurrence of full breast feeding and any breast feeding at discharge and at six months post discharge, and of full (but not any) breast feeding at three months post discharge. This effect was evident at all time points for the tube alone strategy and for all except any breast feeding at three months post discharge for cup feeding. Investigators reported no clear benefit when the novel teat was used. No other benefits or harms were evident, including, in contrast to the previous (2008) review, length of hospital stay.

Authors' conclusions

Evidence of low to moderate quality suggests that supplementing breast feeds by cup increases the extent and duration of breast feeding. Current insufficient evidence provides no basis for recommendations for a tube alone approach to supplementing breast feeds.

PLAIN LANGUAGE SUMMARY

Avoidance of bottles during the establishment of breast feeds in preterm infants

Review question: In preterm infants whose mothers want to breast feed, does using bottles interfere with breast feeding success?

Background: Preterm infants start milk feeds by tube, and as they mature they are able to manage sucking feeds. The number of sucking feeds each day is gradually increased as the baby matures. Women who choose to breast feed their preterm infant may find that it is not always possible to be there every time the baby needs a sucking feed. Conventionally, bottles with mother's milk or formula have been used. It has been suggested that using bottles may interfere with breast feeding success.

Study characteristics: In searches updated to July 2016, we found seven eligible studies (involving 1152 preterm babies). These studies were of small to moderate size, and most had some problems with study design or conduct.

Key results: Five of the studies (which included two of the largest studies) used cup feeds, and one used tube feeds. One study used a specially designed teat with feeding action suggested to be more like breast feeding than conventional bottle feeding. Most studies were conducted in high-income countries, only two in middle-income countries and none in low-income countries. Overall if bottle feeds (with a conventional teat) were not given, babies were more likely to be fully breast fed or to have at least some breast feeds on discharge home and at three and six months after discharge home. The study with the specially designed teat showed no difference in breast feeding outcomes, so it was the cup alone or the tube alone that improved breast feeding rates. However, because of the poor quality of the tube alone study, we cannot recommend a tube feeding strategy until further studies of high quality are undertaken. We found no evidence of benefit or harm for any of the reported outcomes, including length of hospital stay or weight gain.

Conclusions: Using a cup instead of a bottle increases the extent and duration of breast feeding in preterm infants. Additional studies are needed before a tube alone approach can be recommended.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Breast feeding with supplemental feeds by other than bottle compared with breast feeding with supplemental feeds by bottle (all trials) in preterm infants

Breast feeding with supplemental feeds by other than bottle compared with breast feeding with supplemental feeds by bottle (all trials) in preterm infants

Patient or population: preterm infants
Setting:
Intervention: breast feeding with supplemental feeds by other than bottle
Comparison: breast feeding with supplemental feeds by bottle (all trials)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with breast feeding with supplemental feeds by bottle (all trials)	Risk with breast feeding with supplemental feeds by other than bottle				
Full breast feeding at discharge	Study population		RR 1.47 (1.19 to 1.80)	1074 (6 RCTs)	⊕⊕⊖⊖ LOW[a,b]	
	44 per 100	64 per 100 (52 to 79)				
Full breast feeding at 3 months post discharge	Study population		RR 1.56 (1.37 to 1.78)	986 (4 RCTs)	⊕⊕⊕⊖ MODERATE[a]	
	36 per 100	57 per 100 (50 to 65)				
Full breast feeding at 6 months post discharge	Study population		RR 1.64 (1.14 to 2.36)	887 (3 RCTs)	⊕⊕⊖⊖ LOW[a,b]	
	31 per 100	51 per 100 (35 to 73)				
Any breast feeding at discharge	Study population		RR 1.11 (1.06 to 1.16)	1138 (6 RCTs)	⊕⊕⊕⊖ MODERATE[a]	
	79 per 100	88 per 100 (84 to 92)				
Any breast feeding at 3 months post discharge	Study population		RR 1.31 (1.01 to 1.71)	1063 (5 RCTs)	⊕⊖⊖⊖ VERY LOW[a,c]	
	60 per 100	78 per 100 (60 to 100)				

Any breast feeding at 6 months post discharge	Study population		RR 1.25 (1.10 to 1.41)	886 (3 RCTs)	⊕⊖⊖⊖ VERY LOW[a,d]
	45 per 100	56 per 100 (49 to 63)			
Length of hospital stay		MD 2.25 higher (3.36 lower to 7.86 higher)	-	1004 (4 RCTs)	⊕⊖⊖⊖ VERY LOW[a,c]
Episodes of infection	Study population		RR 0.70 (0.35 to 1.42)	500 (3 RCTs)	⊕⊕⊕⊖ MODERATE[a]
	7 per 100	5 per 100 (2 to 10)			

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; OR: odds ratio; RR: risk ratio.

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of effect.
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of effect but may be substantially different.
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of effect.
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

[a]Attrition bias (14% and 15% attrition in two included studies).
[b]Moderate heterogeneity (I^2 = 52%).
[c]Moderate heterogeneity (I^2 = 73%).
[d]Moderate heterogeneity (I^2 = 71%).

BACKGROUND

Description of the condition

Preterm infants begin sucking feeds when they are mature enough to co-ordinate sucking and swallowing; this occurs at around 32 to 34 weeks' gestation (Lemons 1996). Milk feeds are given through a gavage tube until infants are able to receive all their intake by sucking feeds. Once sucking feeds begin, they are increased gradually, usually beginning with once a day and increasing as the infant demands or is assessed as ready to progress. As the number of sucking feeds increases, the number of tube feeds decreases until sucking feeds alone provide sufficient intake for growth and development. It is not always possible for a mother to be available to breast feed during this transition time. Also at times after a breast feed, the infant is assessed as having received insufficient milk, and a 'top up' with expressed breast milk or formula is required. In these instances, it is common clinical practice for milk (breast or formula) to be given by bottle in addition to any breast feeds.

Description of the intervention

Alternatives to bottles during this transition time have been reported and include feeding the infant by cup (Lang 1994a), gavage tube (Stine 1990), finger feeding (Healow 1995; Kurokawa 1994), spoon (Aytekin 2014) and paladai - a traditional feeding device used in India (Malhotra 1999). Increased breast feeding prevalence has been reported when bottle feeds were replaced by cup feeds (Abouelfettoh 2008; Gupta 1999; Lang 1994a) or tube feeds (Stine 1990), and infants have been reported to achieve all breast feeds sooner with spoon feeding (Aytekin 2014). However, these studies were small and did not include a control.

How the intervention might work

It has been suggested that using bottles may interfere with establishing successful breast feeding, possibly because of a difference in the sucking action required for the breast versus an artificial nipple (Bu'Lock 1990; Neifert 1995).

Why it is important to do this review

Alternatives to breast feeds are not necessarily benign. With both bottle feeds (Bier 1993; Blaymore Bier 1997; Chen 2000; Young 1995) and cup feeds (Dowling 2002; Freer 1999), mean oxygen saturation was lower and the frequency of oxygen desaturation was greater than with breast feeding, highlighting the importance of considering safety aspects of any alternatives to bottle feeds. Use of both cup and paladai has been associated with a tendency for infants to 'spill' a large proportion of the feed (Aloysius 2007; Dowling 2002). However, other studies have not reported problems associated with cup feeding (Gupta 1999; Lang 1994a).

Cups and similar feeding vessels are easier to clean than bottles and artificial teats; this fact may be of particular relevance for infection control in low- and middle-income countries.

For women who wish to breast feed their preterm infant, it is important to establish the most efficacious and least harmful method of supplementing breast feeds.

OBJECTIVES

To identify the effects of avoidance of bottle feeds during establishment of breast feeding on the likelihood of successful breast feeding, and to assess the safety of alternatives to bottle feeds.

METHODS

Criteria for considering studies for this review

Types of studies

All trials using random or quasi-random participant allocation.

Types of participants

Infants born at less than 37 weeks' gestation whose mothers had chosen to breast feed, and who had not received 'sucking' feeds by bottle or any alternative feeding device at study entry. At enrolment, infants may have been receiving enteral feeds only, parenteral feeds only or a combination of parenteral and enteral feeds. Their enteral milk intake may have been provided via tube (using expressed breast milk and/or formula) or breast feeds. Tube feeds could be continuous or intermittent, and tube placement could be gastric or duodenal.

Types of interventions

- Experimental intervention: complete avoidance of bottles during the transition to breast feeds. Instead of bottles, alternative feeding devices were used for complementing or supplementing breast feeds, including gavage tube, cup, spoon, dropper, finger feeding, paladai and other.
- Control intervention: breast feeds complemented or supplemented with bottles during the transition to breast feeds.

Types of outcome measures

Primary outcomes

- Full breast feeding compared with not breast feeding or partial breast feeding on discharge home and at three months and six months post discharge
- Any breast feeding (full and partial combined) compared with not breast feeding on discharge home and at three months and six months post discharge

Secondary outcomes

- Time (days) to reach full sucking feeds
- Average rate of weight gain (g/d or g/kg/d) to discharge home
- Length of hospital stay (days)
- Duration (minutes) of supplementary or complementary feed
- Volume of supplementary feed taken compared with volume prescribed (mL)
- Cardiorespiratory stability during and after intervention (mean heart and respiratory rates; proportions of bradycardic and apnoeic events during feed; mean oxygenation measured by oximetry or transcutaneous monitor; proportion of hypoxic events during feed)
- Episodes of choking/gagging per feed
- Milk aspiration on radiological assessment
- Parent/health professional satisfaction with feeding method as measured by self report
- Episodes of infection per infant

Search methods for identification of studies

Electronic searches

We used the criteria and standard methods of The Cochrane Collaboration and the Cochrane Neonatal Review Group (see the Cochrane Neonatal Group search strategy for specialized register).

For the review update in 2016, we conducted a comprehensive search in July 2016 that included the Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 2) in *The Cochrane Library*; MEDLINE via PubMed; Embase; and the Cumulative Index to Nursing and Allied Health Literature (CINAHL), using the following search terms: (cup feed* OR (cup AND feed) OR cupfeed* OR gavage OR (tube AND feed*) OR spoon OR dropper OR (finger AND feed*) OR paladai), plus database-specific limiters for randomised controlled trials (RCTs) and neonates (see Appendix 1 for the full search strategies for each database). We applied no language restrictions.

We searched clinical trials registries for ongoing and recently completed trials (clinicaltrials.gov; the World Health Organization International Trials Registry and Platform www.whoint/ictrp/search/en/ and the ISRCTN Registry).

For the 2008 review, we conducted computerised searches of the Cochrane Central Register of Controlled Trials (CENTRAL; 2007, Issue 4) in *The Cochrane Library*; MEDLINE (1950 to July week 1 2008); the Cumulative Index to Nursing and Allied Health Literature (CINAHL; 1982 to July week 1 2008); and Embase (1980 to 2008 week 28), using medical subject headings (MeSH): breastfeeding; Milk, human; Lactation; Bottle Feeding; Intubation, Gastrointestinal. We used the following text words: Neonat$, Cup, Cup Feed*, Cupfeed*, Gavage, Gavage feed*, Tube feed*, Spoon, Dropper, Finger Feed*, Palada*. We did not restrict the search by language.

Searching other resources

We checked the bibliographies of published trials.

Data collection and analysis

We used standard methods of the Cochrane Neonatal Review Group.

Selection of studies

We merged search results from different databases, using reference management software, and we removed duplicates. One review author (CC) screened titles and abstracts and removed obviously irrelevant reports. Three review authors (CC, HS, JG) independently reviewed the abstracts of potentially relevant reports. When uncertainty about inclusion of the study arose, we retrieved the full text. Review authors (CC, HS, JG) resolved disagreements on inclusion of studies.

Data extraction and management

Once inclusion of trials was established, two review authors (CC, HS) independently assessed trial methods; extracted data onto paper forms; assessed trial quality; and discussed and resolved disagreements (CC, HS).

For the review updated in 2016, we requested additional information from Garpiel 2012 (only abstract available) and from Yilmaz 2014 (gestational age category used in stratification) but received no response. For the 2008 version of this review, we requested additional information from Gilks 2004, Kliethermes 1999 and Rocha 2002. We received additional information from Kliethermes 1999 (on breast feeding prevalence, apnoeic/bradycardic episodes and blinding of assessment outcome) and from Gilks 2004 (on exclusions post randomisation, years study was conducted, type of cup used, days to reach full sucking feeds and milk aspiration).

Assessment of risk of bias in included studies

We used standard methods of The Cochrane Collaboration and the Cochrane Neonatal Review Group to assess the methodological quality of trials (to meet validity criteria). For each trial, we sought information regarding methods of randomisation and blinding and reporting of all outcomes for all infants enrolled. We assessed each criterion as presenting low, high or unclear risk. Two review authors (CC, HS) separately assessed each study and resolved disagreements by discussion. We made explicit judgements about whether studies were at high risk of bias across six domains according to the criteria suggested in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

We included these items for appraisal.

- Random sequence generation and allocation concealment, i.e.
  - random sequence generation: selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence; and
  - allocation concealment: selection bias (biased allocation to interventions) due to inadequate concealment of allocations before assignment.
- Blinding of participants and personnel: performance bias due to knowledge of allocated interventions by participants and personnel during the study.
- Blinding of outcome assessment: detection bias due to knowledge of allocated interventions by outcome assessors.
- Incomplete outcome data: attrition bias due to quantity, nature or handling of incomplete outcome data.
- Selective reporting: reporting bias due to selective outcome reporting.
- Other bias: bias due to problems not covered elsewhere in the table.

See Appendix 2 for a more detailed description of risk of bias for each domain.

We used 'Risk of bias' tables to illustrate risk across trials. We resolved disagreements by consensus and, if necessary, by adjudication with a third review author.

Measures of treatment effect

We analysed treatment effects in individual trials by using Review Manager 5.3. We analysed dichotomous data using risk ratios (RRs), risk difference (RDs) and numbers needed to treat for an additional beneficial outcome (NNTBs) or numbers needed to treat for an additional harmful outcome (NNTHs). We reported 95% confidence intervals (CIs) for all estimates and used mean differences (MDs) with 95% confidence intervals for outcomes measured on a continuous scale. We analysed differences in the number of events for outcomes measured as count data (e.g. episodes of choking/gagging) by comparing rates of events in the two groups.

Unit of analysis issues

The unit of analysis was the participating infant in individually randomised trials.

Dealing with missing data

We requested additional data from trial investigators when data on important outcomes were missing or were reported unclearly. For included studies, we noted levels of attrition. If we had concerns regarding the impact of including studies with high levels of missing data in the overall assessment of treatment effect, we explored this through sensitivity analysis.

We analysed all outcomes on an intention-to-treat basis (i.e. we included in the analyses all participants randomly assigned to each group). The denominator for each outcome in each trial was the number randomly assigned minus any participants whose outcomes were known to be missing.

Assessment of reporting biases

For included trials that were recently performed (and therefore prospectively registered), we explored possible selective reporting of study outcomes by comparing primary and secondary outcomes in the reports versus primary and secondary outcomes proposed at trial registration, using the websites www.clinicaltrials.gov and www.controlled-trials.com.

Data synthesis

We conducted meta-analyses using Review Manager software (RevMan 2014), as supplied by The Cochrane Collaboration. We used the Mantel-Haenszel method to obtain estimates of typical risk ratio and risk difference. For analysis of continuous measures, we used the inverse variance method. For all meta-analyses, we used a fixed-effect model.

Quality of evidence

We used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach, as outlined in the *GRADE Handbook* (Schünemann 2013), to assess the quality of evidence for the following (clinically relevant) outcomes: breast feeding extent and duration, length of hospital stay, growth and episodes of infection.

Two review authors (CC, HS) independently assessed the quality of the evidence for each of the outcomes above. We considered evidence from RCTs as high quality but downgraded the evidence one level for serious (and two levels for very serious) limitations on the basis of the following: design (risk of bias), consistency across studies, directness of the evidence, precision of estimates and presence of publication bias. We used the GRADEpro 2008 Guideline Development Tool to create a 'Summary of findings' table to report the quality of the evidence.

The GRADE approach provides an assessment of the quality of a body of evidence based on four grades.

- High: We are very confident that the true effect lies close to that of the estimate of effect.
- Moderate: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of effect but may be substantially different.
- Low: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of effect.
- Very low: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Subgroup analysis and investigation of heterogeneity

We planned subgroup analyses to determine whether safety and efficacy outcomes were altered by the type of intervention used and the country in which the study took place (low- and middle-income countries vs high-income countries; classified according to http://data.worldbank.org/about/country-classifications). When we found moderate to high heterogeneity (I^2 > 50%), we used a random-effects model and investigated potential sources of the heterogeneity (differences in study quality, participants or treatment regimens). When heterogeneity was explained by subgroup analysis, we presented results in this way.

RESULTS

Description of studies

See also Characteristics of included studies, Characteristics of excluded studies and Characteristics of studies awaiting classification.

Results of the search

We identified and included two new trials, resulting in a total of seven trials included in the review; we excluded 10 studies and found one that awaits classification. We identified no ongoing trials (Figure 1).

Figure 1. Study flow diagram: review update.

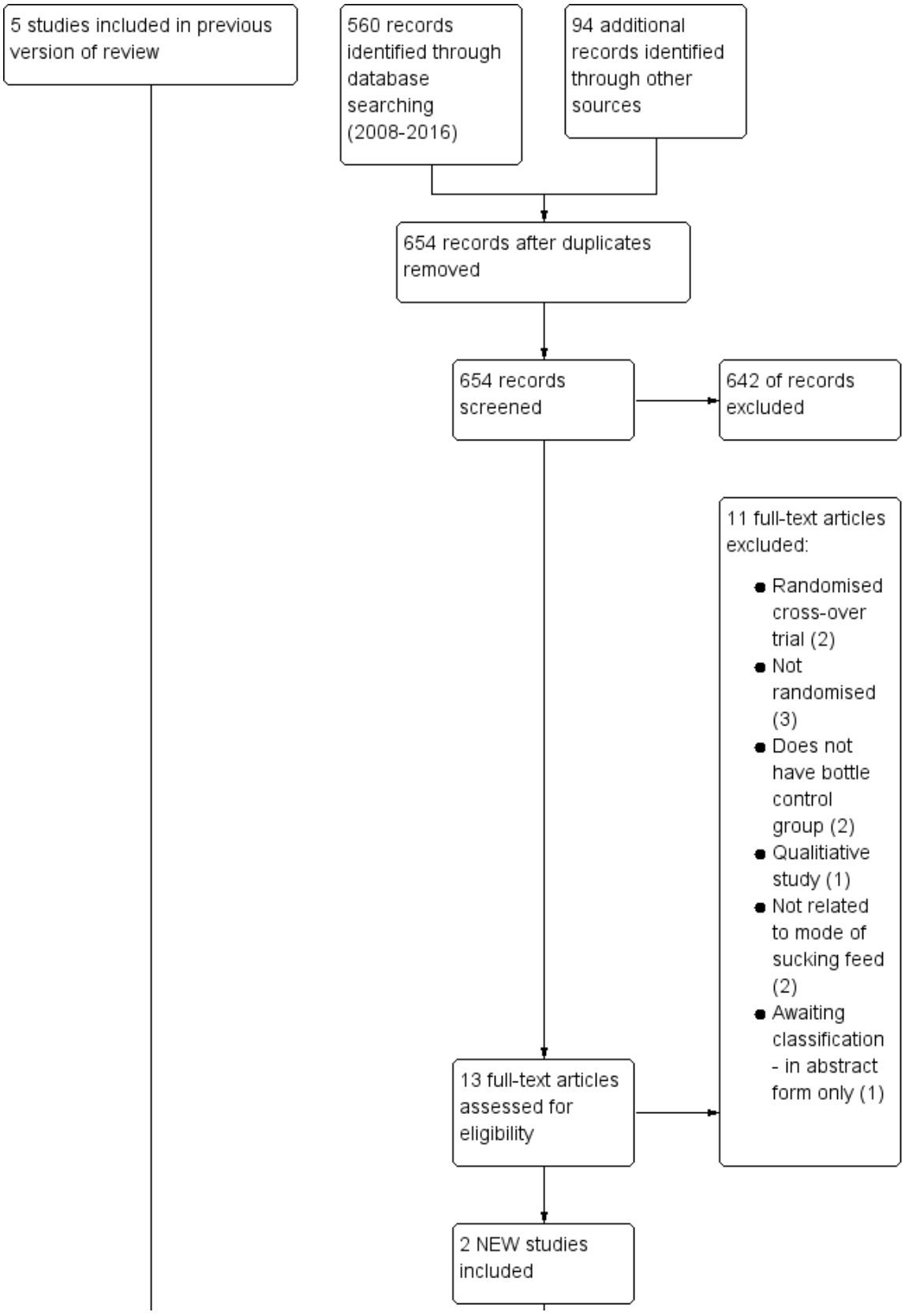
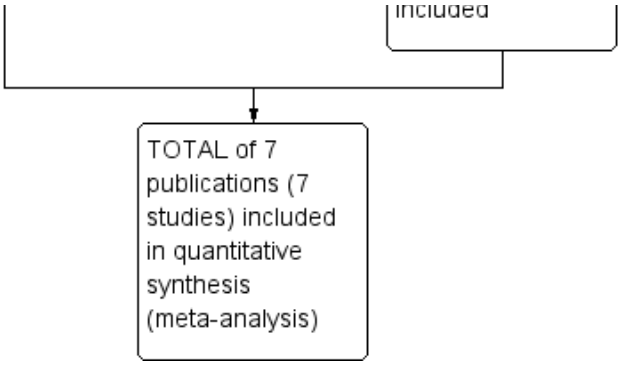


Figure 1. (Continued)



Included studies

We included seven studies and have provided details of each of these studies (Collins 2004; Gilks 2004; Kliethermes 1999; Mosley 2001; Rocha 2002; Simmer 2016; Yilmaz 2014) in the Characteristics of included studies table. Collins 2004 is a primary study report; a PhD thesis presents additional data related to this study (i.e. extent of breast feeding, any and full, at three months and six months post discharge, time to full sucking feeds, weight gain, milk aspiration and reasons for non-compliance). Simmer 2016 is a primary study report that was first published in abstract form. Studies were undertaken in neonatal units in Australia (Collins 2004; Simmer 2016), Brazil (Rocha 2002), England (Gilks 2004; Mosley 2001), Turkey (Yilmaz 2014) and the United States of America (Kliethermes 1999). Five trials were single-centre studies (Gilks 2004; Kliethermes 1999; Mosley 2001; Rocha 2002; Simmer 2016), and two were multi-centre studies (Collins 2004 - two centres; Yilmaz 2014 - three centres).

Participants

This review included a total of 1152 infants; sample sizes ranged from 14 to 522 participants. All studies included preterm infants, although limits for gestational age and birth weight differed. Four studies included extremely preterm and very preterm infants (Collins 2004 < 34 weeks; Rocha 2002 32 to 34 weeks; Gilks 2004 and Simmer 2016 < 35 weeks), and two included moderate to late preterm infants (Mosley 2001 32 to 37 weeks; Yilmaz 2014 32 to 35 weeks); Kliethermes 1999 used a birth weight criterion of 1000 to 2500 grams.

Five studies stratified infants at randomisation - one by birth weight (Rocha 2002) and four by gestational age (Collins 2004; Gilks 2004; Simmer 2016; Yilmaz 2014).

The average gestational age of included infants across all trials was 32 weeks.

Interventions

Those using alternative feeding devices (cup, gavage tube, paladai, finger feeding, dropper, spoon or other) were classified as the experimental group, and infants who received bottle feeding were classified as the control group.

Five studies compared breast feeding with supplementary feeds given by cup versus breast feeding with supplementary feeds given by bottle (Collins 2004; Gilks 2004; Mosley 2001; Rocha 2002; Yilmaz 2014). One trial compared breast feeding with supplementary feeds by bottle versus breast feeding with supplementary feeds by gavage tube alone (Kliethermes 1999). The Simmer 2016 trial used a specially developed feeding system that incorporated a shut-off valve in the teat, so that milk flowed only when the infant created a vacuum; collapse of the teat was prevented by a venting system. Infants controlled the flow of milk by raising the tongue when sucking stopped; study authors (Simmer 2016) showed that this action was similar in breast fed term infants (Geddes 2012). Although this intervention uses a bottle and a teat, the review authors agreed to include this study in the review, given that the 'novel teat' causes action that is purportedly similar to the breast feeding action compared with conventional teats used in all other studies.

In all studies, neither bottle feeds nor alternative feeding devices (cup/tube alone/novel teat) were used to replace a breast feed and were given only when the mother was not available to breast feed, or if extra milk was thought necessary after a breast feed and investigators determined that the infant was able to take this orally.

Among the cup feeding studies, four (Collins 2004; Gilks 2004; Rocha 2002; Yilmaz 2014) followed the cup feeding recommendations of Lang (Lang 1994a; Lang 1994b). Rocha 2002 used the protective cap from a bottle, Collins 2004 and Yilmaz 2014 a 60 mL medicine cup and Gilks 2004 an Ameda baby cup. Mosley 2001 did not state the type of cup used and did not describe the cup feeding procedure. An indwelling nasogastric tube remained in situ for both experimental and control groups in two studies in which feeds were given by tube if insufficient milk was taken during cup or breast feeding, or if the infant was not scheduled for a sucking feed (Collins 2004; Gilks 2004). It is not stated whether this occurred for cup feeds in the other studies (Mosley 2001; Rocha 2002; Yilmaz 2014).

For breast feeding with supplementary feeds by bottle compared with breast feeding with supplementary feeds by gavage tube (Kliethermes 1999), all infants received standard care (including non-nutritive breast feeding) until written orders for oral feedings were given. For the control group, all supplementary feeds were given by bottle, and the indwelling nasogastric tube was removed as directed by the clinical care team. For the experimental group (gavage tube), feeds were given by an indwelling 3.5 gauge French nasogastric tube. The tube was removed during the last 24 to 48 hours of parent 'rooming-in', at which time a cup or syringe was used if needed.

Skin-to-skin contact and non-nutritive sucking at the breast were encouraged for all infants in three studies (Collins 2004; Kliethermes 1999; Simmer 2016). This was not reported in the remaining studies (Gilks 2004; Mosley 2001; Rocha 2002; Yilmaz 2014).

Sucking feeds for experimental and control groups were commenced and advanced according to individual hospital policy. In one trial (Rocha 2002), this decision was based on weight (1600 grams). In Collins 2004, sucking feeds began when infants were assessed as mature enough to co-ordinate a suck-swallow-breathe reflex. In three studies, sucking feeds occurred at the discretion of the nurse or midwife (Collins 2004), the neonatologist (Collins 2004; Kliethermes 1999; Mosley 2001; Yilmaz 2014) or the neonatal nurse practitioner (Kliethermes 1999; Mosley 2001). This information was not reported in Gilks 2004 and Simmer 2016.

Non-nutritive sucking with use of a dummy (also known as a pacifier) varied among the included studies. Collins 2004 randomised infants to cup/no dummy, cup/dummy, bottle/no dummy and bottle/dummy, reporting no statistically significant interaction between infants randomised to no dummy or cup; therefore, results from marginal groups (cup vs bottle and dummy vs no dummy) could be analysed independently. In Kliethermes 1999, a dummy was available during tube feedings for the experimental group, and study authors did not report whether a dummy was available outside feeding times in either group. In Rocha 2002, a dummy was not used for the experimental (cup) group, and Mosley 2001 reported that six infants were given a dummy. In Simmer 2016, non-nutritive sucking was encouraged in both groups, and Gilks 2004 and Yilmaz 2014 did not report dummy use.

Outcomes

All outcomes were not reported in each study.

All studies measured breast feeding outcomes (Collins 2004; Gilks 2004; Kliethermes 1999; Mosley 2001; Rocha 2002; Simmer 2016; Yilmaz 2014). Six studies (Collins 2004; Gilks 2004; Kliethermes 1999; Mosley 2001; Simmer 2016; Yilmaz 2014) measured full breast feeding at discharge home from hospital, four studies (Collins 2004; Kliethermes 1999; Simmer 2016; Yilmaz 2014) at three months post discharge and three studies (Collins 2004; Kliethermes 1999; Yilmaz 2014) at six months post discharge.

Six studies (Collins 2004; Gilks 2004; Kliethermes 1999; Rocha 2002; Simmer 2016; Yilmaz 2014) measured any breast feeding at discharge home from hospital, five studies (Collins 2004; Kliethermes 1999; Rocha 2002; Simmer 2016; Yilmaz 2014) at three months post discharge and three studies (Collins 2004; Kliethermes 1999; Yilmaz 2014) at six months post discharge.

Three studies (Collins 2004; Kliethermes 1999; Yilmaz 2014) used the following definition of full breast feeding: No other solids or liquids were given apart from vitamins, minerals, juice or ritualistic feedings, given infrequently. Mosley 2001 used the term 'exclusive' and Simmer 2016 'fully' breast feeding but did not define the terms; however, these investigators reported both breast feeding and breast milk feeds. Rocha 2002 defined breast feeding as feeding exclusively or partially directly at the breast. Kliethermes 1999 and Gilks 2004 considered infants who were receiving supplementary feeds of expressed breast milk on discharge as partially breast fed, and Collins 2004 considered them fully breast fed. Two per cent of women (n = 6) with 2% of infants (n = 7) in Collins 2004 had chosen to feed their infants expressed breast milk by bottle; researchers randomised three to cup feeds and four to bottle feeds.

At three months and six months post discharge, Collins 2004 used the term 'all breast feeds' to indicate that an infant's milk feeds were breast feeds only when no other types of milk were given, and 'partial breast feeds' to mean that an infant's milk feeds were a combination of breast feeds and other types of milk. The intent was to determine the types of milk feeds infants were receiving (breast or formula), irrespective of whether they were receiving solids. This does not fit with the conventional definition of full breast feeding (Labbok 1990), that is, if an infant is on solids and all milk feeds are breast feeds, the infant is usually classified as 'partially' breast feeding. The Collins 2008 review did not include data for 'all breast feeds' in the meta-analyses. Given the small number of studies reporting this outcome, review authors reconsidered and have included the data for 'all breast feeds' in the meta-analysis in this 2016 update.

Three studies (Collins 2004; Gilks 2004; Simmer 2016) measured the time taken to reach full sucking feeds. Three studies (Collins 2004; Rocha 2002; Yilmaz 2014) reported rate of weight gain, four (Collins 2004; Kliethermes 1999; Simmer 2016; Yilmaz 2014) length of hospitalisation and two (Rocha 2002; Yilmaz 2014) supplementary feeding time. No studies reported the volume of supplementary feed taken compared with the volume prescribed.

Two studies reported cardiorespiratory stability. Kliethermes 1999 reported apnoeic or bradycardic episodes, and Rocha 2002 oxygen saturation associated with mode of feeding. No studies reported episodes of choking/gagging, and two trials reported milk aspiration (Collins 2004; Gilks 2004). Collins 2004 reported parental satisfaction, and three studies (Collins 2004; Kliethermes 1999; Simmer 2016) reported episodes of infection.

Excluded studies

See Characteristics of excluded studies for details. We excluded:

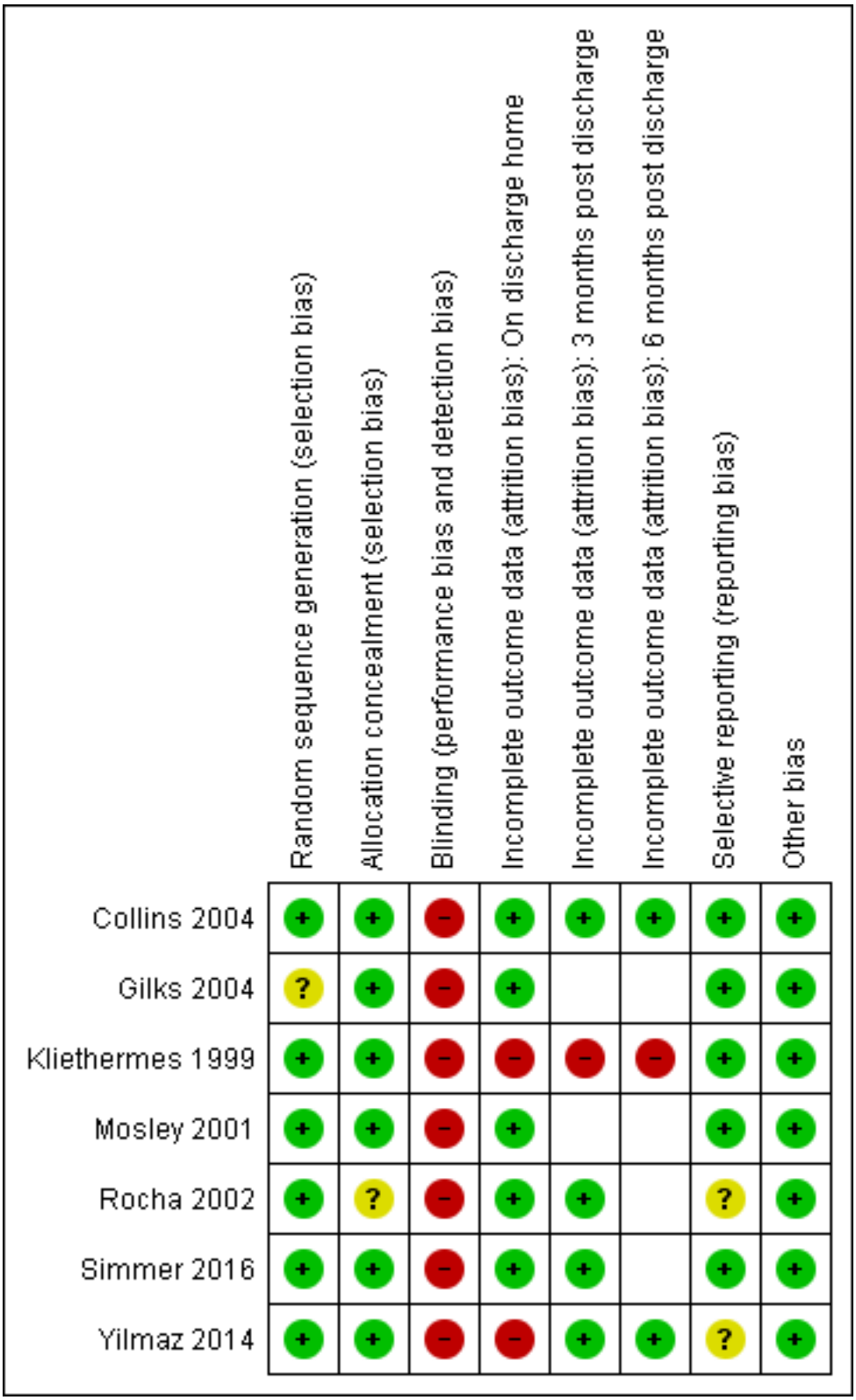
- Abouelfettoh 2008, Aytekin 2014, De Aquino 2009, Harding 2014, Lau 2012 and Ronan 2013 because they were not RCTs;
- Aloysius 2007 and Lopez 2014 because they were randomised cross-over trials; and
- Kumar 2010 and Marofi 2016 because they did not include a bottle control group.

One study (Garpiel 2012) is awaiting classification.

Risk of bias in included studies

We have provided details of the methodological quality of each study in the Characteristics of included studies table (Figure 2).

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Risk of selection bias was low with adequate methods of random sequence generation described in six studies (Collins 2004; Kliethermes 1999; Mosley 2001; Rocha 2002; Simmer 2016; Yilmaz 2014) and not described in Gilks 2004. Allocation concealment was adequate in six studies (Collins 2004; Gilks 2004; Kliethermes 1999;

Mosley 2001; Simmer 2016; Yilmaz 2014) and was unclear in Rocha 2002.

Blinding

Risk of performance and detection bias was high, as blinding of treatment was not possible in any study. Five studies (Kliethermes 1999; Mosley 2001; Rocha 2002; Simmer 2016; Yilmaz 2014) did not clearly state whether outcome assessment was blinded. Two studies (Collins 2004; Gilks 2004) stated that data for outcomes were collected unblinded. Simmer 2016 was the only study that described blinding of analyses.

Incomplete outcome data

We judged risk of bias due to incomplete outcome data as low in six studies (Collins 2004; Gilks 2004; Mosley 2001; Rocha 2002; Simmer 2016; Yilmaz 2014) and high in Kliethermes 1999. Studies handled protocol violations differently; five studies excluded the infants from analyses (Gilks 2004; Kliethermes 1999; Mosley 2001; Rocha 2002; Yilmaz 2014). Proportions of incomplete outcome data for the primary outcome were as follows: Collins 2004 5%, Gilks 2004 0%. Kliethermes 1999 15%, Mosley 2001 13%, Rocha 2002 6%, Simmer 2016 3% and Yilmaz 2014 14%.

Collins 2004 reported a high proportion of non-compliance. In the experimental (cup) group, 85 of 151 (56%) had a bottle introduced, and in the control group, 1 of 152 (0.7%) had a cup introduced. Infants were analysed in the group to which they were randomised (Collins 2004).

Selective reporting

We found no evidence of reporting bias.

Other potential sources of bias

We found no evidence of other potential sources of bias.

Effects of interventions

See: **Summary of findings for the main comparison** Breast feeding with supplemental feeds by other than bottle compared with breast feeding with supplemental feeds by bottle (all trials) in preterm infants

See Summary of findings for the main comparison. Breast feeding with supplemental feeds by other than bottle versus breast feeding with supplemental feeds by bottle.

This review includes seven studies with 1152 infants.

We conducted subgroup analyses to determine whether outcomes were altered by type of intervention. We incorporated the subgroups into the main structure of each figure.

Full breast feeding (Outcomes 1.1 to 1.3)

At discharge home (Analysis 1.1)

Six studies reported this outcome in 1074 infants (Collins 2004; Gilks 2004; Kliethermes 1999; Mosley 2001; Simmer 2016; Yilmaz 2014). Three trials (Collins 2004; Kliethermes 1999; Yilmaz 2014) as well as the meta-analysis of data from all trials showed a statistically significantly higher rate of full breast feeding in the experimental (avoid bottle) group (typical risk ratio (RR) 1.47, 95% confidence interval (CI) 1.19 to 1.80; risk difference (RD) 0.21, 95% CI 0.09 to 0.32; number needed to treat for an additional beneficial outcome (NNTB) 5, 95% CI 3 to 11). Heterogeneity between studies was moderate (I^2 = 52%).

Subgroup analyses by intervention type: full breast feeding at discharge home (Outcomes 1.1.1 to 1.1.3)

The subgroup interaction test was not statistically significantly different, although the P value = 0.08 indicates that the effect on breast feeding of a tube alone approach may have a more significant impact on breast feeding success than a cup feeding approach. However, only one small study with high risk of bias (Kliethermes 1999) used a tube alone feeding approach.

Four studies with 893 infants (Collins 2004; Gilks 2004; Mosley 2001; Yilmaz 2014) compared cup feeds with bottle feeds. The statistically significant increase in full breast feeding remained (typical RR 1.41, 95% CI 1.14 to 1.75; RD 0.20, 95% CI 0.10 to 0.308; NNTB 5, 95% CI 3 to 10) with low heterogeneity (I^2 = 45%). Kliethermes 1999 showed a significant increase in full breast feeding (tube alone vs bottle), and Simmer 2016 when comparing different teats showed no difference in full breast feeding.

Three months post discharge (Analysis 1.2)

Four studies (Collins 2004; Kliethermes 1999; Simmer 2016; Yilmaz 2014) with 986 infants reported this outcome. Two studies (Kliethermes 1999; Yilmaz 2014) and the meta-analysis showed a statistically significantly higher rate of full breast feeding in the experimental (avoid bottle) group (typical RR 1.56, 95% CI 1.37 to 1.78; RD 0.20, 95% CI 0.15 to 0.26; NNTB 5, 95% CI 4 to 7). We detected low heterogeneity in this analysis (I^2 = 37%).

Subgroup analyses by intervention type: full breast feeding at three months post discharge (Outcomes 1.2.1 to 1.2.3)

Cup feeding compared with bottle feeding (Collins 2004; Yilmaz 2014) showed a significant increase in full breast feeding (typical RR 1.54, 95% CI 1.34 to 1.77; RD 0.21, 95% CI 0.15 to 0.27; NNTB 5, 95% CI 4 to 7) but with moderate heterogeneity (I^2 = 61%). Setting, participants and risk of bias differed in the two cup feeding studies. Collins 2004 was conducted in a high-income country, included more immature infants (mean gestational age, 30 weeks) and reported low adherence with the intervention and overall low risk of bias, whereas Yilmaz 2014 included more mature infants (mean gestational age, 33 weeks) and high adherence with the intervention, was conducted in a high-middle-income country and had high risk of attrition bias. Kliethermes 1999 reported that tube alone versus bottle showed increased full breast feeding, and Simmer 2016 described no differences when different teats were compared.

Six months post discharge (Analysis 1.3)

Full breast feeding was significantly increased at six months post discharge in the experimental (avoid bottle) group in both individual trials and the meta-analysis (887 infants, three studies: Collins 2004; Kliethermes 1999; Yilmaz 2014) (typical RR 1.64, 95% CI 1.14 to 2.36; RD 0.15, 95% CI 0.07 to 0.24; NNTB 7, 95% CI 4 to 14). Moderate heterogeneity was detected (I^2 = 52%).

Subgroup analyses by intervention type: full breast feeding at six months home (Outcomes 1.3.1 to 1.3.3)

Tube alone versus bottle statistically significantly increased full breast feeding (Kliethermes 1999). The subgroup interaction test

(P = 0.06) indicated that the effect on breast feeding of the tube alone approach (Kliethermes 1999) may have a more significant impact on breast feeding success than the cup feeding approach, as described above. The two cup feeding trials (Collins 2004; Yilmaz 2014) noted an increase in full breast feeding in the cup group (typical RR 1.54, 95% CI 1.34 to 1.77; RD 0.13, 95% CI 0.07 to 0.19, NNTB 8, 95% CI 5 to 14) with no heterogeneity (I^2= 0%).

Any breast feeding (Outcomes 1.4 to 1.6)

At discharge home (Analysis 1.4)

Data were obtained from six trials including 1138 infants (Collins 2004; Gilks 2004; Kliethermes 1999; Rocha 2002; Simmer 2016; Yilmaz 2014). Two studies (Kliethermes 1999; Yilmaz 2014) as well as the meta-analysis showed a statistically significantly higher rate of any breast feeding on discharge home in the experimental (avoid bottle) group (typical RR 1.11, 95% CI 1.06 to 1.16; RD 0.09, 95% CI 0.05 to 0.13; NNTB 11, 95% CI 8 to 20) with no heterogeneity detected.

Subgroup analyses by intervention type: any breast feeding at discharge home (Outcomes 1.4.1 to 1.4.3)

One of the cup feeding studies (Yilmaz 2014) and the meta-analysis revealed a significant increase in breast feeding (Collins 2004; Gilks 2004; Rocha 2002; Yilmaz 2014; 957 infants; typical RR 1.09, 95% CI 1.03 to 1.15; RD .07, 95% CI .03 to .11; NNTB 14. 95% CI 9 to 33, no heterogeneity), as did the tube alone trial (Kliethermes 1999), but Simmer 2016 noted no such increase upon comparing two different types of teats.

Three months post discharge (Analysis 1.5)

Five studies with 1063 infants (Collins 2004; Kliethermes 1999; Rocha 2002; Simmer 2016; Yilmaz 2014) contributed data to this outcome. Two studies (Kliethermes 1999; Rocha 2002) and a meta-analysis of data showed a statistically significant increase in the rate of any breast feeding in the experimental (avoid bottle) group (typical RR 1.31, 95% CI 1.01 to 1.71; RD 0.14, 95% CI 0.04 to 0.24; NNTB 7, 95% CI 4 to 25), with moderate heterogeneity detected (I^2 = 73%).

Subgroup analyses by intervention type: any breast feeding at three months post discharge (Outcomes 1.5.1 to 1.5.3)

Researchers found no clear benefit of cup feeding for any breast feeding at three months post discharge (883 infants, three trials; Collins 2004; Rocha 2002; Yilmaz 2014). Tube alone showed a statistically significant increase in any breast feeding (Kliethermes 1999) but with no statistically significant differences between novel and conventional teats (Simmer 2016).

Six months post discharge (Analysis 1.6)

Three studies with 886 infants (Collins 2004; Kliethermes 1999; Yilmaz 2014) provided data on this outcome. Two studies (Kliethermes 1999; Yilmaz 2014) and a meta-analysis showed a statistically significant increase in the rate of any breast feeding at six months post discharge in experimental (avoid bottle) groups (typical RR 1.25, 95% CI 1.10 to 1.41; RD 0.11, 95% CI 0.05 to 0.17; NNTB 9, 95% CI 6 to 20), with moderate heterogeneity detected (I^2 = 50%).

Subgroup analyses by intervention type: any breast feeding at three months post discharge (Outcomes 1.6.1 to 1.6.3)

Cup feeding in Collins 2004 and Yilmaz 2014 (803 infants) resulted in a statistically significant increase in any breast feeding at six months post discharge (typical RR 1.20, 95% CI 1.06 to 1.36; RD 0.09, 95% CI 0.03 to 0.16; NNTB 11, 95% CI 6 to 22) with no heterogeneity. Tube alone also showed a statistically significant increase in any breast feeding (Kliethermes 1999). The subgroup interaction test P value = 0.06 in Kliethermes 1999 indicated that the effect on breast feeding of a tube alone approach may have a more significant impact on breast feeding success than a cup feeding approach. However, only one small study with high risk of bias used a tube alone approach.

Time (days) to reach full sucking feeds (Outcome 1.7)

Four studies measured this outcome (Analysis 1.7) in 513 infants (Collins 2004; Gilks 2004; Kliethermes 1999; Simmer 2016). Two studies (Collins 2004; Kliethermes 1999) showed a significant increase in days to reach full sucking feeds in the experimental (avoid bottle) group. Kliethermes 1999 did not report standard deviations, so their data could not be included in the meta-analysis; however, the increase (7.5 days) was of the same magnitude as reported in Collins 2004 (10.5 days). Meta-analysis (Collins 2004; Gilks 2004; Simmer 2016) revealed no clear effect on days to taken to reach full sucking feeds in the experimental (avoid bottle) group.

Subgroup analyses by intervention type: time (days) to reach full sucking feeds (Outcomes 1.7.1, 1.7.2)

Neither the two cup feeding trials (Collins 2004; Gilks 2004; 332 infants) nor the novel teat feeding trial (Simmer 2016) showed a clear increase or reduction in days to reach full sucking feeds. The tube alone study (Kliethermes 1999) reported a significant increase in days to reach full sucking feeds.

Weight gain (g/kg/d or g/d) (Outcome 1.8)

Three studies with 893 infants (all cup) reported no statistically significant differences in weight gain (g/kg/d; Analysis 1.8) when measured from birth to discharge home (Collins 2004), or one week after oral feeds were commenced (Rocha 2002; Yilmaz 2014). A meta-analysis was not possible because different units of measurement were used. Simmer 2016 reported that infants in the experimental (novel teat) group were statistically significantly lighter on discharge home (mean difference (MD) -186 grams, 95% CI -317 to -56).

Length of hospital stay, days (Outcome 1.9)

We obtained data from four studies with 1004 infants (Analysis 1.9) (Collins 2004; Kliethermes 1999; Simmer 2016; Yilmaz 2014). Collins 2004 showed a statistically significant increase in length of hospital stay of 10 days with the experimental (cup) group, but meta-analysis revealed no statistically significant difference (MD 2.25, 95% CI -3.36 to 7.86 days). Moderate heterogeneity was present in this analysis (I^2 = 73%).

Subgroup analyses by intervention type: length of hospital stay (days) (Outcomes 1.9.1 to 1.9.3)

The two cup feeding trials with 823 infants (Collins 2004; Yilmaz 2014) showed no clear difference in length of hospital stay (MD 4.45, 95% CI -5.57 to 14.48 days). High heterogeneity was present (I^2 = 90%). The overall length of stay differed between these studies

owing to differences in the maturity of included infants. Collins 2004 suggested that increased length of stay may have been related to problems with staff and acceptance by parents of cup feeding, with some infants less satisfied and more difficult to feed by cup as they matured, resulting in feeding by tube and delayed onset of all sucking feeds - a requirement for discharge home. Kliethermes 1999 (tube alone) and Simmer 2016 (novel teat) also showed no statistically significant differences in length of hospital stay.

Duration (minutes) of supplementary feed (Outcome 1.10)

Two studies with 600 infants (Rocha 2002; Yilmaz 2014; both cup intervention) measured duration of supplementary feeds and showed no significant differences in time taken to cup feed versus time taken to bottle feed (MD -0.42, 95% CI -1.96 to 1.12 minutes). Moderate heterogeneity was present in this analysis (I^2 = 60%) (Analysis 1.10) and is not explained by the maturity of included infants, as infants in both studies were at a mean of 33 weeks' gestation.

Episodes of infection (Outcome 1.11)

Three studies with 500 infants reported infection (Analysis 1.11): Collins 2004 reported necrotising enterocolitis; Kliethermes 1999 reported infection not defined; and Simmer 2016 reported late-onset sepsis. All participants were from high-income countries, and neither trials nor the meta-analysis showed a statistically significant difference in episodes of infection (typical RR 0.70, 95% CI 0.35 to 1.42). No heterogeneity was detected.

Cardiorespiratory stability

One trial (Kliethermes 1999) reported the total number of episodes of apnoea and bradycardia per infant. Researchers described significantly fewer apnoeic and bradycardic incidents for the experimental (tube alone) group (mean 127, SD not reported) compared with the control (bottle) group (mean 136, SD not reported; P = 0.0006). However, the breast feeding plus bottle group had significantly more episodes requiring stimulation (mean 32.7 episodes, SD not reported vs mean 23.3 episodes, SD not reported; P = 0.0001). Investigators measured apnoeic and bradycardic episodes over the entire hospital stay - not just episodes associated with feeding. Rocha 2002 reported mean oxygen saturation during feeds and showed no statistically significant difference in the mean of the lowest oxygen saturation during feeds (cup mean 90.8, SD 4.8, range 75 to 99; bottle mean 87.7, SD 7.6, range 68 to 97). Rocha 2002 also reported oxygen desaturation during feeds and showed no difference in desaturation episodes of less than 90% with cup feeds (18/44, 40.9%) compared with the bottle group (19/34, 55.9%). Researchers reported a statistically significant difference in the proportion of desaturation episodes less than 85%, with fewer occurring in cup groups (6/44, 13.6%) than in bottle groups (12/34, 35.3%; P = 0.02).

Milk aspiration on radiological assessment

The three studies that reported this outcome (Collins 2004; Gilks 2004; Yilmaz 2014) described no episodes of milk aspiration.

Satisfaction with feeding method

One study included views of parents on the method of feeding (Collins 2004) and noted a high rate of non-compliance, with 56% of infants in the intervention (breast feeding with supplemental feeds by cup) group (n = 85/151) having a bottle introduced. Compliance differed between recruiting hospitals; the hospital at which cup feeding was introduced specifically for this study had a higher rate of compliance than the other recruiting hospital, where cup feeding had been practised for three years before the study began. Researchers collected data on reasons for the introduction of a bottle from the medical records or after discussion with attending nurses or midwives. Reasons for introducing a bottle were available for 74% (n = 63) of the 85 infants randomised to cup feeds who had a bottle introduced. In 65% (n = 41) of cases, the reason given for introduction of a bottle was that it was introduced at the request of the mother, and the staff initiated the bottle in 29% (n = 18) of cases. In 10% (n = 6) of cases, researchers introduced a bottle because the baby was not satisfied with cup feeds or would not settle down. One infant randomised to the bottle group had a cup introduced because of transfer to a peripheral hospital, where cup feeding was routinely done.

The three month post discharge questionnaire included a question to the mother on reasons for introduction of a bottle. Reasons for introducing a bottle were available for 91% (n = 77) of the 85 infants randomised to cup feeds who had a bottle introduced. Women could select from a list of options, and additional space was provided for any other comments. A total of 44% (n = 34) indicated that the decision to introduce a bottle was theirs, and 33% (n = 25) were advised by the nurse or midwife (some responded yes to both of these statements). In all, 26% (n = 20) had problems with cup feeding including inability of the infant to do it, frequent spills, dissatisfaction with cup feeds and unacceptably long feeding times. Ten (13%) of the respondents did not like cup feeds and changed feeding method because of this. Nine (12%) respondents said that the staff refused to cup feed their infant. Collins 2004 reported that some infants became less satisfied with cup feeds and more difficult to feed by this method as they neared discharge, generally during the last week of their hospital stay. Because of this, if the mother could not be present to breast feed, the infant would be tube fed. The criterion for discharge home was that the infant had to be on full sucking feeds. This may have contributed to increased length of stay in this study. However, the study author cautions that reliable data on this point were not collected (Collins 2004).

Outcomes not reported

No studies reported the volume of supplementary feed taken compared with the volume prescribed, nor did they describe episodes of choking or gagging.

Subgroup analysis: trials conducted in low- and middle-income countries

Two trials were conducted in upper-middle-income countries: Rocha 2002 in Brazil and Yilmaz 2014 in Turkey. Meta-analyses were limited and showed no substantial differences from the meta-analysis of all trials together (Analysis 1.1; Analysis 1.2; Analysis 1.3; Analysis 1.4; Analysis 1.5; Analysis 1.6; Analysis 1.8; Analysis 1.9; Analysis 1.10). These studies did not report infection rates.

DISCUSSION

Summary of main results

The strategy of avoiding bottles while an infant breast feeds is being established in preterm infants, resulting in statistically significant increases in the extent and duration of breast feeding. Studies included in this review compared cup feeding with a tube alone

approach or a novel teat versus bottle feeding with a conventional teat. Across all time points (discharge home, three months and six months post discharge), both a cup feeding strategy and a tube alone strategy increased breast feeding success. We included the novel teat study in this review, as the design of the teat, in which a vacuum is created, attempted to mimic the sucking action required for breast feeding, thereby potentially supporting breast feeding success when compared with a conventional teat. Investigators found no differences in breast feeding outcomes with the novel teat, rather the cup and tube alone studies reported an increase in breast feeding. Meta-analysis of data from trials that included length of stay, weight gain and infection showed no clear evidence of benefit or harm. Limited evidence from the two trials that assessed cardiorespiratory stability suggests improved stability with avoidance of bottles.

Overall completeness and applicability of evidence

The trials reviewed provide no information on the volume of feed consumed compared with the volume prescribed nor on episodes of choking/gagging per feed. We found limited information on cardiorespiratory stability and parent and health professional satisfaction with the feeding method. No studies were conducted in low-income countries, and two were completed in middle-income countries. No reports describe infants dissatisfied with tube or cup, except Collins 2004, in which adherence with cup feeding was poor. In contrast, cup feeding had not previously been used in Yilmaz 2014, and staff acceptance was high, with high adherence to the intervention. Both of the largest studies were cup feeding studies, but they were conducted in different populations and settings. Collins 2004 was conducted in a high-income country in very and extremely preterm infants, whereas Yilmaz 2014 included moderate to late preterm infants in a high-middle-income country. Lang 1997 suggested that as preterm infants mature, they may be able to bottle feed with no interference with breast feeds, but she cautions that the introduction of a bottle should occur only when breast feeding is well established. Such a strategy might be more acceptable to staff and parents, but no randomised controlled trials have investigated this approach.

Quality of the evidence

We included in this review seven studies with 1152 infants. Blinding was not possible in any of the included studies and therefore was subject to caregiver influence. We graded the level of evidence for full breast feeding as low or moderate, and for any breast feeding as moderate or very low (Summary of findings for the main comparison). We graded the level of evidence for episodes of infection and length of hospital stay as moderate and very low (Summary of findings for the main comparison). We downgraded outcomes because of attrition and moderate to high heterogeneity. The direction of effects of all included trials was consistent (favouring avoiding bottles) for breast feeding outcomes, but the magnitude of effects in Kliethermes 1999 was inconsistent with that in the other studies. The most likely reason for this heterogeneity was the difference in the intervention provided or the poorer quality of the study. Kliethermes 1999 used supplemental feeding by tube, and Simmer 2016 a novel teat, whereas the remaining trials used supplemental feeds by cup. Heterogeneity was considerable between cup feeding studies that reported length of stay (Collins 2004; Yilmaz 2014), with length of stay increased by a mean of 10 days in Collins 2004, and no difference was reported in Yilmaz 2014.

Potential biases in the review process

Assessment of risk of bias involves subjective judgements. Review authors therefore independently assessed studies and resolved disagreements through discussion (Higgins 2011). We attempted to identify all relevant studies by screening the reference lists of included trials and related reviews.

AUTHORS' CONCLUSIONS

Implications for practice

We found evidence of improved breast feeding rates when breast feeds are supplemented with cup feeds, with higher rates of full and any breast feeding at discharge and at six months post discharge, and higher rates of any (but not full) breast feeding at three months post discharge. We found insufficient evidence on which to base recommendations for supplementing breast feeds with a tube alone strategy, and we found evidence suggesting that a novel teat does not clearly confer breast feeding benefit.

Implications for research

The heterogeneity of the included studies reveals the need for well-conducted studies of both cup feeding and a tube alone strategy. Such studies should evaluate length of hospital stay, weight gain, breast feeding prevalence on discharge home and at three months and six months post discharge and infection episodes, as well as infant, parent and staff satisfaction with the feeding method.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Collins 2004

Methods	Randomised controlled trial, stratified by gestational age < 28 weeks and 28 to < 34 weeks and by study centre. Study duration - 3 years, 1996 to 1999
Participants	Two Australian Neonatal Intensive Care Units Inclusion criteria: gestational age < 34 weeks (experimental: mean 29.4 weeks, SD 2.6, range 23 to 33; control: mean 30.0 weeks, SD 2.5, range 24 to 33), mother wishes to breast feed, infant had not been fed by cup or bottle, no congenital abnormality precluding sucking feeds, dummy use ≤ 48 hours Sample size: 319 randomised (161 experimental/cup, 158 control/bottle). 303 included in analysis (151 experimental/cup, 152 control/bottle)
Interventions	Randomised to cup/no dummy, cup/dummy, bottle/no dummy, bottle/dummy Experimental: supplementary feeds given by cup according to Lang 1994b recommendations; 60 mL medicine cup used Control: supplementary feeds given by bottle Both groups: Infants breast fed when mother was present; cup/bottle was used in addition to nasogastric tube.
Outcomes	Breast feeding prevalence any and full at discharge, and 'all' and any at 3 and 6 months; days to all sucking feeds; length of hospitalisation; weight gain from birth to discharge home; necrotising enterocolitis
Notes	Initial analyses showed no clinically important nor significant interaction between use of cups and dummies; therefore, additional comparisons were performed on marginal groups with cup vs bottle. High proportion of non-compliance: experimental group: 85/151 (46%) had a bottle introduced; control group: 1/152 (0.7%) had a cup introduced. Participants were analysed in the groups to which they were randomised regardless of the intervention they actually received.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "An independent researcher developed a separate randomisation schedule for each recruiting hospital by using a random number table to select balanced blocks of varying size with stratification for gestation (< 28 weeks, 28 - < 34 weeks)".
Allocation concealment (selection bias)	Low risk	Quote: "Assignments were sealed in sequentially numbered, opaque envelopes. Researchers determined allocation by telephoning an independent ward, available 24 hours a day, within the recruiting hospitals".
Blinding (performance bias and detection bias) All outcomes	High risk	Quote: "Particpants, care providers, and researchers were not blinded to treatment allocation; data entry and analysis were undertaken unblinded". Comment: blinding of intervention not possible

Collins 2004 *(Continued)*

Incomplete outcome data (attrition bias) On discharge home	Low risk	Missing outcome data (n = 16, 5%) due to attrition (experimental 10, control 6): • Deaths 4: experimental 8, control 4 • Withdrawals 4: 2 in each group Comment: low risk of bias due to incomplete outcome data
Incomplete outcome data (attrition bias) 3 months post discharge	Low risk	Missing outcome data (n = 36, 11%) due to attrition (experimental 17, control 19): • Deaths 4: experimental 8, control 4 • Withdrawals 4: 2 in each group • Inability to locate 20: experimental 7, control 13 Comment: low risk of bias due to incomplete outcome data
Incomplete outcome data (attrition bias) 6 months post discharge	Low risk	Missing outcome data (n = 38, 12%) due to attrition (experimental 19, control 19): • Deaths 4: experimental 8, control 4 • Withdrawals 4: 2 in each group • Inability to locate 22: 9 experimental, 13 control Comment: low risk of bias due to incomplete outcome data
Selective reporting (reporting bias)	Low risk	Before clinical trial registration requirements; however, outcomes reported as per PhD thesis
Other bias	Low risk	

Gilks 2004

Methods	Randomised controlled trial, stratified by gestational age < 31 weeks and 31 to < 35 weeks. Study duration - 2 years, 2002 to 2004
Participants	Single centre, Neonatal Intensive Care Unit, UK Inclusion criteria: < 35 weeks' gestation (experimental: median 31 weeks, range 25 to 34; control: median 32 weeks, range 26 to 34 weeks), > 30 weeks' postmenstrual age at trial entry, ability to tolerate full strength, full volume of nasogastric feeds for 48 hours or longer, anticipated stay ≥ 1 week, mother's intention to breast feed Sample size: 54 randomised, 54 included in analysis (additional information from study author). Number randomised to each group: 27 (experimental/cup), 27 (control/bottle)
Interventions	Experimental: supplementary feeds given by cup when mother not present to breast feed Control: supplementary feeds given by bottle when mother not present to breast feed Both groups: Infants breast fed when mother was present; cup/bottle was used in addition to nasogastric tube.
Outcomes	Breast feeding prevalence any and full on discharge home, at term and at 6 weeks post term; postmenstrual age at nasogastric tube withdrawal
Notes	

Gilks 2004 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: “randomized, non-blinded stratified controlled trial" Comment: unable to determine whether sequence generation was adequate
Allocation concealment (selection bias)	Low risk	Quote: "randomization was by selection of concealed cards in envelopes, stratified by gestation"
Blinding (performance bias and detection bias) All outcomes	High risk	Quote: “randomized, non-blinded stratified controlled trial" Quote (from correspondence): "No one was blinded in the study once the envelope was opened". Comment: blinding of intervention not possible
Incomplete outcome data (attrition bias) On discharge home	Low risk	3 infants not accounted for in paper, additional information provided by study author 14 women counted as withdrawals in the paper, as they no longer wanted to breast feed. With additional information from study author, reanalysed in this review Comment: outcome data complete
Selective reporting (reporting bias)	Low risk	Before clinical trial registration requirements, all expected outcomes were reported.
Other bias	Low risk	Nil noted

Kliethermes 1999

Methods	Randomised controlled trial. Study duration - 22 months
Participants	Single centre, Neonatal Intensive Care Unit, USA Inclusion criteria: birth weight 1000 g to 2500 g, < 1 week of age, no congenital or neurological abnormalities that interfered with cardiopulmonary status Gestational age at birth - experimental: 32 weeks, SD not reported, range 26 to 35 weeks; control: 32 weeks, SD not reported, range 28 to 35 weeks; birth weight - experimental: 1.73 kg, range 1.05 kg to 2.43 kg; control: 1.64 kg, range 1.0 kg to 2.35 kg; twins - experimental: 8 (21%); control: 16 (35%) Sample size: 99 randomised (47 experimental/tube alone, 52 control/bottle); 84 included in analysis (38 experimental/tube alone, 46 control/bottle)
Interventions	Both groups of infants breast fed when mother was present. Experimental group: feeds given by indwelling size 3.5 FG nasogastric tube when mother not available, or top-up after breast feed required. Tube was removed during last 24 to 48 hours of parent 'rooming-in' period; a cup or syringe was used during this time if needed. Control group: fed by bottle when mother not available, or top-up after breast feed required. Indwelling nasogastric tube was removed as directed by clinicians.
Outcomes	Breast feeding, exclusive and partial, at discharge home, and at 3 days, 3 months and 6 months post discharge. Length of hospital stay, apnoea/bradycardia, weight gain to discharge home, infection rate

Kliethermes 1999 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was achieved by using sealed envelopes, which were physically mixed and drawn in random sequence after enrolment of the dyad into the study".
Allocation concealment (selection bias)	Low risk	Quote: "...sealed envelopes"
Blinding (performance bias and detection bias) All outcomes	High risk	Comment: Blinding of intervention not possible. Blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) On discharge home	High risk	Missing outcome data (n = 15, 15%) (experimental 9, control 6): • Deaths 1: experimental • Clinical conditions 4: experimental 2 (chronic lung disease, congenital heart defect); control 2 (NEC, subglottic stenosis) • Transfer to another hospital 2: 1 in each group • Protocol violation 5: experimental 3, control 2 • Maternal conditions 3: experimental 2 (scleroderma, +ve cocaine screen), control 1 (+ve cocaine screen) Comment: high risk of bias due to incomplete outcome data. Difference in proportion of missing data across groups (19% experimental, 12% control). For 4 infants, valid reasons were given for missing outcome data (1 died, 2 were transferred to another hospital).
Incomplete outcome data (attrition bias) 3 months post discharge	High risk	Missing outcome data (n = 15, 15%) (experimental 9, control 6): • Deaths 1: experimental • Clinical conditions 4: experimental 2 (chronic lung disease, congenital heart defect); control 2 (NEC, subglottic stenosis) • Transfer to another hospital 2: 1 in each group • Protocol violation 5: experimental 3, control 2 • Maternal conditions 3: experimental 2 (scleroderma, +ve cocaine screen), control 1 (+ve cocaine screen) Comment: high risk of bias due to incomplete outcome data
Incomplete outcome data (attrition bias) 6 months post discharge	High risk	Missing outcome data (n = 15, 15%) (experimental 9, control 6): • Deaths 1: experimental • Infant clinical conditions 4: experimental 2 (chronic lung disease, congenital heart defect); control 2 (NEC, subglottic stenosis) • Transfer to another hospital 2: 1 in each group • Protocol violation 5: experimental 3, control 2 • Maternal conditions 3: experimental 2 (scleroderma, +ve cocaine screen), control 1 (+ve cocaine screen) Comment: high risk of bias due to incomplete outcome data

Kliethermes 1999 *(Continued)*

Selective reporting (reporting bias)	Low risk	Before clinical trial registration requirements, all expected outcomes reported
Other bias	Low risk	Nil noted

Mosley 2001

Methods	Randomised controlled trial, pilot study. Study duration - 3 months
Participants	Single centre, Special Care Baby Unit, District General Hospital, England Inclusion criteria: gestational age 32 to 37 weeks, mother wishes to breast feed, no congenital abnormality, no maternal preference for cup or bottle, infant had not been fed by cup or bottle Experimental group: mean gestational age 35.5 weeks, SD not reported; control group: 35.2 weeks, SD not reported Sample size: 16 randomised (8 experimental/cup, 8 control/bottle); 14 included in analysis (6 experimental/cup, 8 control/bottle)
Interventions	Experimental: supplementary feeds given by cup Control: supplementary feeds given by bottle
Outcomes	Prevalence exclusive breast feeding on discharge home
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "There were 10 instructions to cup feed and ten to bottle feed. These details were then put in the envelopes, shuffled thoroughly and then the envelopes were numbered sequentially".
Allocation concealment (selection bias)	Low risk	Quote: "Midwife/nurse responsible was asked to select a sealed, numbered, opaque envelope, which contained information on the feeding method to be adopted".
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind intervention. No information provided on blinding of outcome assessors
Incomplete outcome data (attrition bias) On discharge home	Low risk	Missing outcome data (n = 2, 13%) (experimental 2, control 0): • Protocol violation (Quote: "excluded from the study prior to its start....had been given a supplementary feed") Comment: Although difference in proportion of incomplete outcome data was noted across groups (25% experimental, 0% control), the sample size was so small that we are unable to sensibly assess the impact of missing data. Low risk of bias due to incomplete outcome data
Selective reporting (reporting bias)	Low risk	Before clinical trial registration requirements, all expected outcomes reported

Mosley 2001 *(Continued)*

Other bias	Low risk	Nil noted

Rocha 2002

Methods	Randomised controlled trial, stratified by weight (500 to 999 g, 1000 to 1499 g, 1500 to 1699 g). Study duration - 18 months, August 1998 to February 2000
Participants	Single centre, Neonatal Intensive Care Unit, University Hospital, Brazil Inclusion criteria: gestational age at birth 32 to 34 weeks (experimental: mean 32.7 weeks, SD 1.8, range not reported; control: mean 32.5 weeks, SD 2, range not reported) and birth weight < 1700g (experimental: mean 1276 g, SD 283 g; control: mean 1262 g, SD 270 g), mothers wished to breast feed, clinically stable, not initially on parenteral nutrition Sample size: 83 randomised (46 experimental/cup, 37 control/bottle); 78 included in analysis (44 experimental/cup, 34 control/bottle)
Interventions	Infants in both groups fed by orogastric tube until 1600 g. Experimental: supplements or complements given by cup according to the recommendations of Kuehl 1997 and Lang 1994a. Dummy not offered. Control: supplements or complements given by bottle
Outcomes	Breast feeding prevalence on discharge, at first follow-up visit and at 3 months post discharge. Weight gain (calculated as the difference between weight at the beginning of the intervention and weight at the end of 1 week during feeding observation, reported in g/kg/d). Length of feeding time (1 week after beginning oral feeds). Oxygen saturation Breast feeding was defined as an infant exclusively or partially breast fed directly at the breast.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: ". controlled experimental study with stratified randomisation"; "Within each stratum, the infants were randomly assigned to 1 of 2 feeding groups by drawing lots".
Allocation concealment (selection bias)	Unclear risk	Quote: "Infants were randomly assigned to 1 of 2 feeding groups by drawing lots". Comment: Mechanism for drawing of lots not reported, therefore unclear whether allocation was concealed
Blinding (performance bias and detection bias) All outcomes	High risk	Blinding of intervention not possible. Blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) On discharge home	Low risk	Missing outcome data (n = 5, 6%) (experimental 2, control 3): • Control 3: gastro-oesophageal reflux, bronchopulmonary dysplasia, maternal cocaine use • Experimental 2: protocol violation, bronchopulmonary dysplasia Comment: low risk of bias due to incomplete outcome data. Small difference in proportions of missing data across groups, although protocol violations on-

Rocha 2002 *(Continued)*

		ly in experimental group (4% experimental, 8% control). Overall small proportion of missing data (6%)
Incomplete outcome data (attrition bias) 3 months post discharge	Low risk	Missing outcome data (n = 5, 6%) (experimental 2, control 3): • Control 3: gastro-oesophageal reflux, bronchopulmonary dysplasia, maternal cocaine use • Experimental 2: protocol violation, bronchopulmonary dysplasia Comment: low risk of bias due to incomplete outcome data. Small difference in proportions of missing data across groups, although protocol violations only in experimental group (4% experimental, 8% control). Overall small proportion of missing data (6%)
Selective reporting (reporting bias)	Unclear risk	Before clinical trial registration requirements, all expected outcomes reported
Other bias	Low risk	

Simmer 2016

Methods	Randomised controlled trial, stratified by 25 to 29 weeks' and 30 to 33 weeks' gestational age. Twins randomised to same group. Conducted from 1 August 2011 to 30 June 2012
Participants	Single centre, Neonatal Intensive Care Unit, Australia Inclusion criteria: gestational age 25 to 34 weeks (experimental: 30.1, SD 2.7 weeks, birth weight 1310, SD 422 g; control: 30.1, SD 2.6 weeks, birth weight 1430, SD 507 g); mother intended to breast feed; required 75% enteral feeds by intragastric tube with remainder provided by parental nutrition Exclusion criteria: congenital anomalies, grade 4 intracerebral haemorrhage, periventricular leukomalacia, oral anomalies (e.g. ankyloglossia, cleft palate) Sample size: 100 randomised (54 experimental/novel teat, 46 control/bottle with conventional teat), 97 included in analysis (51 experimental/novel teat, 46 control/bottle with conventional teat)
Interventions	Bottles were offered only if a bottle feed was scheduled, and duration of feed was limited to 30 minutes. Non-nutritive sucking encouraged up to 33 weeks before suck feeds, after which increasing suck feeds replaced non-nutritive sucking Experimental: a feeding system (Medela AG, Baar, Switzerland) that combined strategies known to improve oral feeding skills: development of vacuum and self paced feeding. A shut-off valve incorporated in the system to ensure that milk flowed only when infant created a vacuum; venting prevented collapse of the teat. Two different threshold levels for the valve of -10, SD 5 mmHg and -30, SD 15 mmHg Control: conventional teat that allowed milk flow with gravity and compression of the teat (Grow, Growbaby, Icon Health, Victoria, Australia, or Peristaltic Narrow Neck Slow Flow, Pigeon, Seoul, South Korea)
Outcomes	Primary outcomes: time to first and full suck feeds, length of hospital stay, breast feeding (full and any) at discharge Secondary outcomes: breast feeding rates (full and any) at 3, 6 and 12 weeks post discharge, late-onset sepsis
Notes	The manufacturer of the feeding system (Medela AG, Baar, Switzerland) provides an unrestricted research grant from which the salaries of 2 authors were paid; the research nurse was partially funded by the manufacturer.

Simmer 2016 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: " ....computer generated treatment allocation..."
Allocation concealment (selection bias)	Low risk	Quote: "...sealed opaque coded envelopes containing the computer generated treatment allocation were sequentially numbered for randomization"
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind families and staff. Analysis done by biostatistician who was not involved in data collection and was blinded to treatment allocation
Incomplete outcome data (attrition bias) On discharge home	Low risk	Missing outcome data (n = 3, 3%) (experimental 3, control 0): • Experimental 3: withdrew (triplets) Comment: low risk of bias due to incomplete outcome data
Incomplete outcome data (attrition bias) 3 months post discharge	Low risk	As above
Selective reporting (reporting bias)	Low risk	Prospectivley registered on clinical trial register, all outcomes reported
Other bias	Low risk	Nil noted

Yilmaz 2014

Methods	Randomised controlled trial with stratification by gestation (gestational age stratification category not stated) Study conducted April 2006 to February 2008
Participants	Three Neonatal Intensive Care Units, Turkey Inclusion criteria: singleton birth, 32 to 35 weeks' gestation (experimental: gestation 32.8, SD 0.9 weeks, birth weight 1539, SD 332; control: 32.8, SD 0.9, birth weight 1547, SD 330), maternal intention to breast feed, no supplemental oxygen required, fed intermittently by gastric tube only at the time of recruitment Exclusion criteria*:* no prerandomisation exclusion criteria stated. Infants excluded post randomisation have been listed in the exclusion criteria (development of a disease that prevented oral feeding for more than 2 consecutive days and non-compliance with assigned feed method). Sample size: 607 randomised (299 experimental/cup, 308 control/bottle); 522 included in analysis (254 experimental/cup, 268 control/bottle
Interventions	Infants in both randomised groups were breast fed whenever the mother was available; mothers were welcome to stay in the NICU 24 hours a day and had access to a comfortable chair/recliner, bed, or mattress while nursing. If supplementation required once home, the same assigned method was used (cup or bottle). Experimental: supplementary feeds (formula or breast milk) given by cup (small plastic medicine cup) by NICU nurses or parents who had been trained in the cup feeding technique described by Lang 1994a

Yilmaz 2014 *(Continued)*

	Control: supplementary feeds (formula or breast milk) given by bottle by nursing staff or parents
Outcomes	Primary: weight gain (g/d) at day 7 of study; proportion of exclusively or any breast fed infants on discharge home Secondary: length of hospital stay and proportion of exclusive or any breast feeding at 3 and 6 months of age. Also reported feeding time (min/feeding during first week of study for cup or bottle)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Separate randomisation schedule for each recruiting hospital by using a random number table to select balanced blocks of varying size with stratification for gestation"
Allocation concealment (selection bias)	Low risk	Quote: "Assignments were sealed in sequentially numbered, opaque envelopes".
Blinding (performance bias and detection bias) All outcomes	High risk	Unable to blind assigned treatment groups Primary outcome data collected by researcher from data recorded in medical records Secondary outcome assessment data collection at 3 and 6 months post discharge collected at home visit, not blinded
Incomplete outcome data (attrition bias) On discharge home	High risk	Missing outcome data: 85/607 (14%) (45/299, 15%, experimental (cup); and 40/308, 13%, control (bottle)): • Non-compliance: 8% (47/607) (26/299, 9%, experimental (cup); and 21/308, 7%, control (bottle) group • Development of clinical condition preventing oral feeding for more than 2 days: 6% (38/607) (19/299, 6% experimental (cup) and 19/308, 6%, control (bottle)) Missing outcome data: 14%; reasons missing similar between groups
Incomplete outcome data (attrition bias) 3 months post discharge	Low risk	No further missing data - as for discharge home
Incomplete outcome data (attrition bias) 6 months post discharge	Low risk	No further missing data - as for discharge home
Selective reporting (reporting bias)	Unclear risk	Trial registration not reported in manuscript. All expected outcomes reported
Other bias	Low risk	Nil noted

FG: French gauge.
NEC: necrotising enterocolitis.
NICU: neonatal intensive care unit.
SD: standard deviation.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abouelfettoh 2008	Not randomised. Thirty infants received usual practice (bottle supplementation), and the next 30 the intervention (supplementation using cup feeds).
Aloysius 2007	Randomised cross-over study. Infants fed by paladai or bottle on consecutive feeds. The aim of the study was to assess amount of spillage, volume consumed, time taken and physiological stability during both a cup feed and a bottle feed.
Aytekin 2014	Not randomised. Aim was to determine effects of spoon feeding compared with bottle feeding on breast feeding success. Conducted in 2 neonatal intensive care units - 1 that used bottle feeds and 1 that used spoon feeds
De Aquino 2009	Not randomised, a retrospective study
Harding 2014	Involves non-nutritive sucking only, not related to mode of sucking feeds nor to breast feeding outcomes
Kumar 2010	Randomised groups do not include a bottle group; nasogastric tube alone compared with spoon feeding
Lau 2012	Involves sucking and swallowing exercises, not related to mode of sucking feeds nor to breast feeding outcomes
Lopez 2014	Randomised cross-over trial. Assessed swallowing and spilling when fed by cup and by bottle during first sucking feed only; did not include breast feeding outcomes
Marofi 2016	Randomised groups do not include a bottle group, have compared feeding by cup with feeding by paladay (paladai)
Ronan 2013	Qualitative study

Characteristics of studies awaiting assessment *[ordered by study ID]*

Garpiel 2012

Methods	Four-group, parallel, randomised controlled trial
Participants	132 infants born at 26 to 36 weeks' gestation
Interventions	Randomised to 1 of 4 groups: (1) nasogastric tube with pacifier, (2) bottle with preterm teat, (3) cup feeding with 30 mL medicine cup, (4) Haberman infant feeder (Medela)
Outcomes	Primary outcome: breast feeding ability at discharge and tolerance to supplementary method of feeding Secondary outcomes: breast feeding rate at discharge, at 2 and 4 weeks post discharge; weight gain; hospital length of stay; frequency of skin-to-skin contact; maternal satisfaction with the feeding method
Notes	Abstract only; review authors have attempted to contact the study author

DATA AND ANALYSES

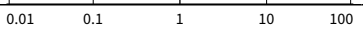
Comparison 1. Breast feeding with supplemental feeds by other than bottle versus breast feeding with supplemental feeds by bottle (all trials)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Full breast feeding at discharge	6	1074	Risk Ratio (M-H, Random, 95% CI)	1.47 [1.19, 1.80]
1.1 Breast feeding + Cup vs Breast feeding + Bottle	4	893	Risk Ratio (M-H, Random, 95% CI)	1.41 [1.14, 1.75]
1.2 Breast feeding + Tube vs Breast feeding + Bottle	1	84	Risk Ratio (M-H, Random, 95% CI)	2.10 [1.46, 3.03]
1.3 Breast feeding + novel teat and bottle vs Breast feeding + conventional teat and bottle	1	97	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.63, 1.82]
2 Fully breast feeding at 3 months post discharge	4	986	Risk Ratio (M-H, Fixed, 95% CI)	1.56 [1.37, 1.78]
2.1 Breast feeding + Cup vs Breast feeding + Bottle	2	805	Risk Ratio (M-H, Fixed, 95% CI)	1.54 [1.34, 1.77]
2.2 Breast feeding + Tube vs Breast feeding + Bottle	1	84	Risk Ratio (M-H, Fixed, 95% CI)	2.31 [1.28, 4.17]
2.3 Breast feeding + novel teat and bottle vs Breast feeding + conventional teat and bottle	1	97	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [0.57, 2.41]
3 Fully breast feeding at 6 months post discharge	3	887	Risk Ratio (M-H, Random, 95% CI)	1.64 [1.14, 2.36]
3.1 Breast feeding + Cup vs Breast feeding + Bottle	2	803	Risk Ratio (M-H, Random, 95% CI)	1.40 [1.18, 1.65]
3.2 Breast feeding + Tube vs Breast feeding + Bottle	1	84	Risk Ratio (M-H, Random, 95% CI)	2.94 [1.36, 6.34]
4 Any breast feeding at discharge	6	1138	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [1.06, 1.16]
4.1 Breast feeding + Cup vs Breast feeding + Bottle	4	957	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [1.03, 1.15]
4.2 Breast feeding + Tube vs Breast feeding + Bottle	1	84	Risk Ratio (M-H, Fixed, 95% CI)	1.37 [1.08, 1.74]
4.3 Breast feeding + novel teat and bottle vs Breast feeding + conventional teat and bottle	1	97	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.95, 1.33]
5 Any breast feeding at 3 months post discharge	5	1063	Risk Ratio (M-H, Random, 95% CI)	1.31 [1.01, 1.71]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Breast feeding + Cup vs Breast feeding + Bottle	3	883	Risk Ratio (M-H, Random, 95% CI)	1.24 [0.89, 1.71]
5.2 Breast feeding + Tube vs Breast feeding + Bottle	1	83	Risk Ratio (M-H, Random, 95% CI)	1.69 [1.19, 2.41]
5.3 Breast feeding + novel teat and bottle vs Breast feeding + conventional teat and bottle	1	97	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.80, 1.80]
6 Any breast feeding at 6 months post discharge	3	886	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [1.10, 1.41]
6.1 Breast feeding + Cup vs Breast feeding + Bottle	2	803	Risk Ratio (M-H, Fixed, 95% CI)	1.20 [1.06, 1.36]
6.2 Breast feeding + Tube vs Breast feeding + Bottle	1	83	Risk Ratio (M-H, Fixed, 95% CI)	2.07 [1.18, 3.64]
7 Days to reach full sucking feeds	3	429	Mean Difference (IV, Random, 95% CI)	2.56 [-7.17, 12.28]
7.1 Breast feeding + Cup vs Breast feeding + Bottle	2	332	Mean Difference (IV, Random, 95% CI)	5.08 [-6.43, 16.59]
7.2 Breast feeding + novel teat and bottle vs Breast feeding + conventional teat and bottle	1	97	Mean Difference (IV, Random, 95% CI)	-4.0 [-15.63, 7.63]
8 Weight gain	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
8.1 Measured from birth to discharge home (g/kg/day)	1	293	Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.77, 0.59]
8.2 Measured for one week after commencing oral feeds (g/kg/day)	1	78	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-3.21, 2.01]
8.3 Measured for one week after commencing oral feeds (g/day)	1	522	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.36, 0.16]
9 Length of hospital stay	4	1004	Mean Difference (IV, Random, 95% CI)	2.25 [-3.36, 7.86]
9.1 Breast feeding + Cup vs Breast feeding + Bottle	2	823	Mean Difference (IV, Random, 95% CI)	4.45 [-5.57, 14.48]
9.2 Breast feeding + Tube vs Breast feeding + Bottle	1	84	Mean Difference (IV, Random, 95% CI)	1.60 [-5.89, 9.09]
9.3 Breast feeding + novel teat and bottle vs Breast feeding + conventional teat and bottle	1	97	Mean Difference (IV, Random, 95% CI)	-4.90 [-17.25, 7.45]
10 Duration of supplementary feed	2	600	Mean Difference (IV, Random, 95% CI)	-0.42 [-1.96, 1.12]
11 Episodes of infection	3	500	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.35, 1.42]

Analysis 1.1. Comparison 1 Breast feeding with supplemental feeds by other than bottle versus breast feeding with supplemental feeds by bottle (all trials), Outcome 1 Full breast feeding at discharge.

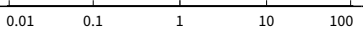
Study or subgroup	BF + avoid bottle n/N	BF + bottle n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Breast feeding + Cup vs Breast feeding + Bottle					
Collins 2004	92/151	72/152		27.92%	1.29[1.04,1.59]
Gilks 2004	10/27	4/27		3.68%	2.5[0.89,7]
Mosley 2001	4/6	6/8		7.3%	0.89[0.44,1.78]
Yilmaz 2014	184/254	123/268		32.5%	1.58[1.36,1.83]
Subtotal (95% CI)	**438**	**455**		**71.4%**	**1.41[1.14,1.75]**
Total events: 290 (BF + avoid bottle), 205 (BF + bottle)					
Heterogeneity: Tau^2=0.02; Chi^2=5.46, df=3(P=0.14); I^2=45.06%					
Test for overall effect: Z=3.19(P=0)					
1.1.2 Breast feeding + Tube vs Breast feeding + Bottle					
Kliethermes 1999	33/38	19/46		17.66%	2.1[1.46,3.03]
Subtotal (95% CI)	**38**	**46**		**17.66%**	**2.1[1.46,3.03]**
Total events: 33 (BF + avoid bottle), 19 (BF + bottle)					
Heterogeneity: Not applicable					
Test for overall effect: Z=3.98(P<0.0001)					
1.1.3 Breast feeding + novel teat and bottle vs Breast feeding + conventional teat and bottle					
Simmer 2016	19/51	16/46		10.95%	1.07[0.63,1.82]
Subtotal (95% CI)	**51**	**46**		**10.95%**	**1.07[0.63,1.82]**
Total events: 19 (BF + avoid bottle), 16 (BF + bottle)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.25(P=0.8)					
Total (95% CI)	**527**	**547**		**100%**	**1.47[1.19,1.8]**
Total events: 342 (BF + avoid bottle), 240 (BF + bottle)					
Heterogeneity: Tau^2=0.03; Chi^2=10.42, df=5(P=0.06); I^2=52%					
Test for overall effect: Z=3.61(P=0)					
Test for subgroup differences: Chi^2=5.09, df=1 (P=0.08), I^2=60.74%					



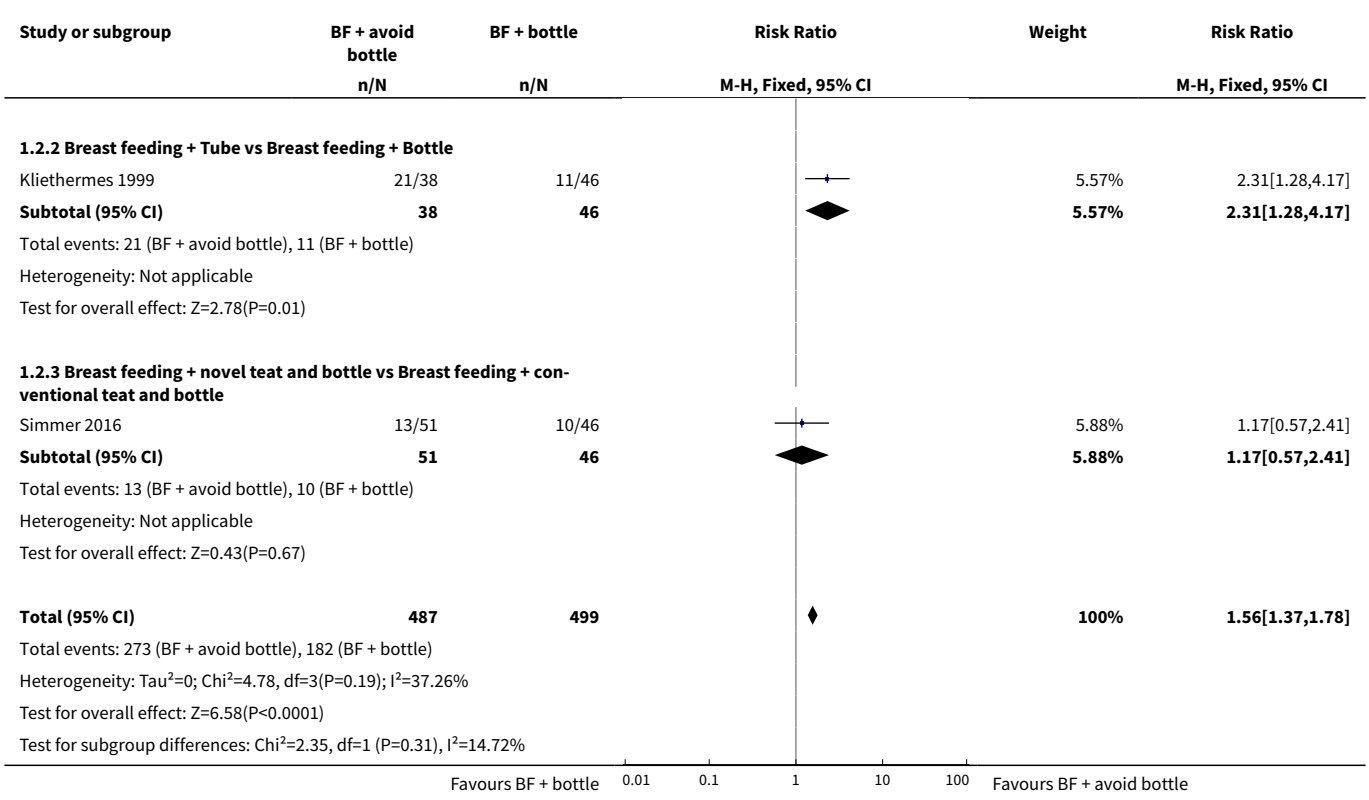
Favours BF + bottle — Favours BF + avoid bottle

Analysis 1.2. Comparison 1 Breast feeding with supplemental feeds by other than bottle versus breast feeding with supplemental feeds by bottle (all trials), Outcome 2 Fully breast feeding at 3 months post discharge.

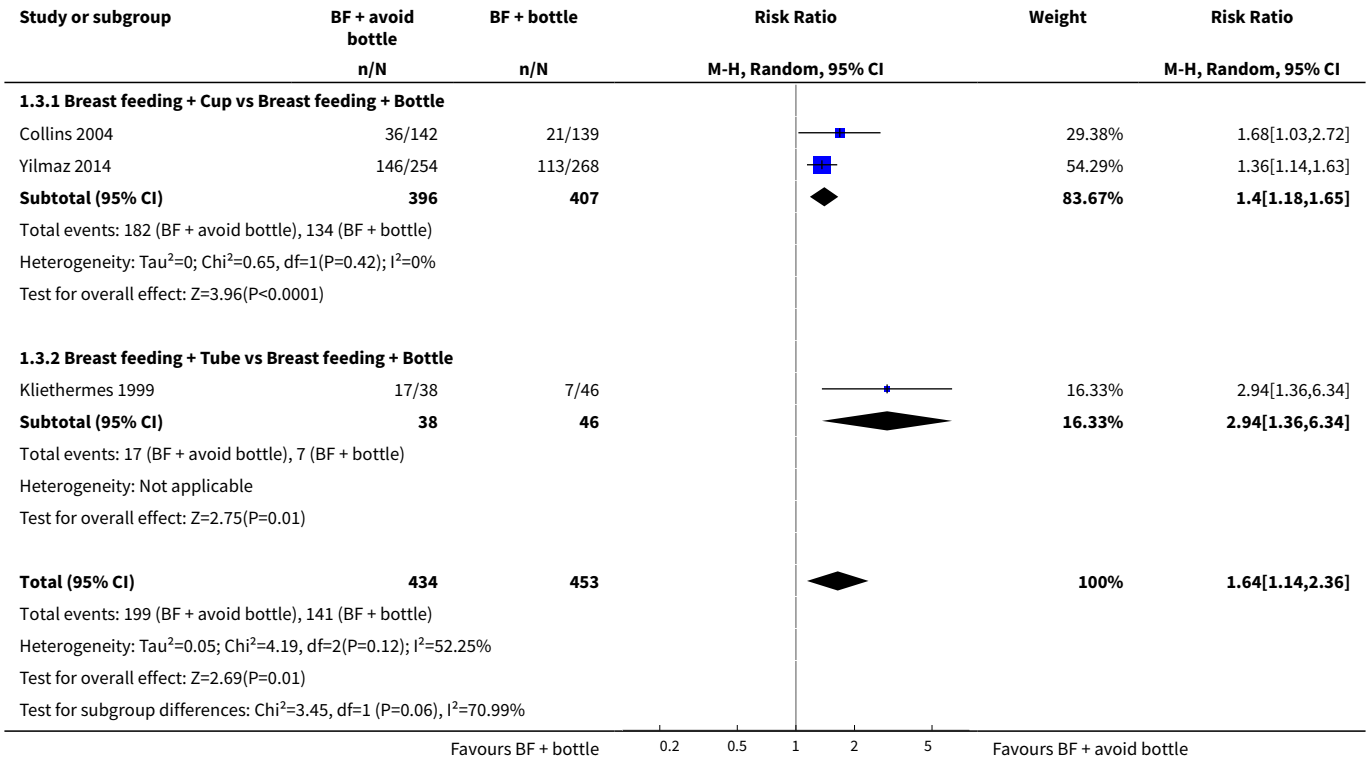
Study or subgroup	BF + avoid bottle n/N	BF + bottle n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 Breast feeding + Cup vs Breast feeding + Bottle					
Collins 2004	43/144	35/139		19.93%	1.19[0.81,1.74]
Yilmaz 2014	196/254	126/268		68.62%	1.64[1.42,1.89]
Subtotal (95% CI)	**398**	**407**		**88.55%**	**1.54[1.34,1.77]**
Total events: 239 (BF + avoid bottle), 161 (BF + bottle)					
Heterogeneity: Tau^2=0; Chi^2=2.57, df=1(P=0.11); I^2=61.16%					
Test for overall effect: Z=6.15(P<0.0001)					



Favours BF + bottle — Favours BF + avoid bottle

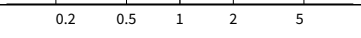


Analysis 1.3. Comparison 1 Breast feeding with supplemental feeds by other than bottle versus breast feeding with supplemental feeds by bottle (all trials), Outcome 3 Fully breast feeding at 6 months post discharge.



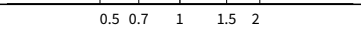
Analysis 1.4. Comparison 1 Breast feeding with supplemental feeds by other than bottle versus breast feeding with supplemental feeds by bottle (all trials), Outcome 4 Any breast feeding at discharge.

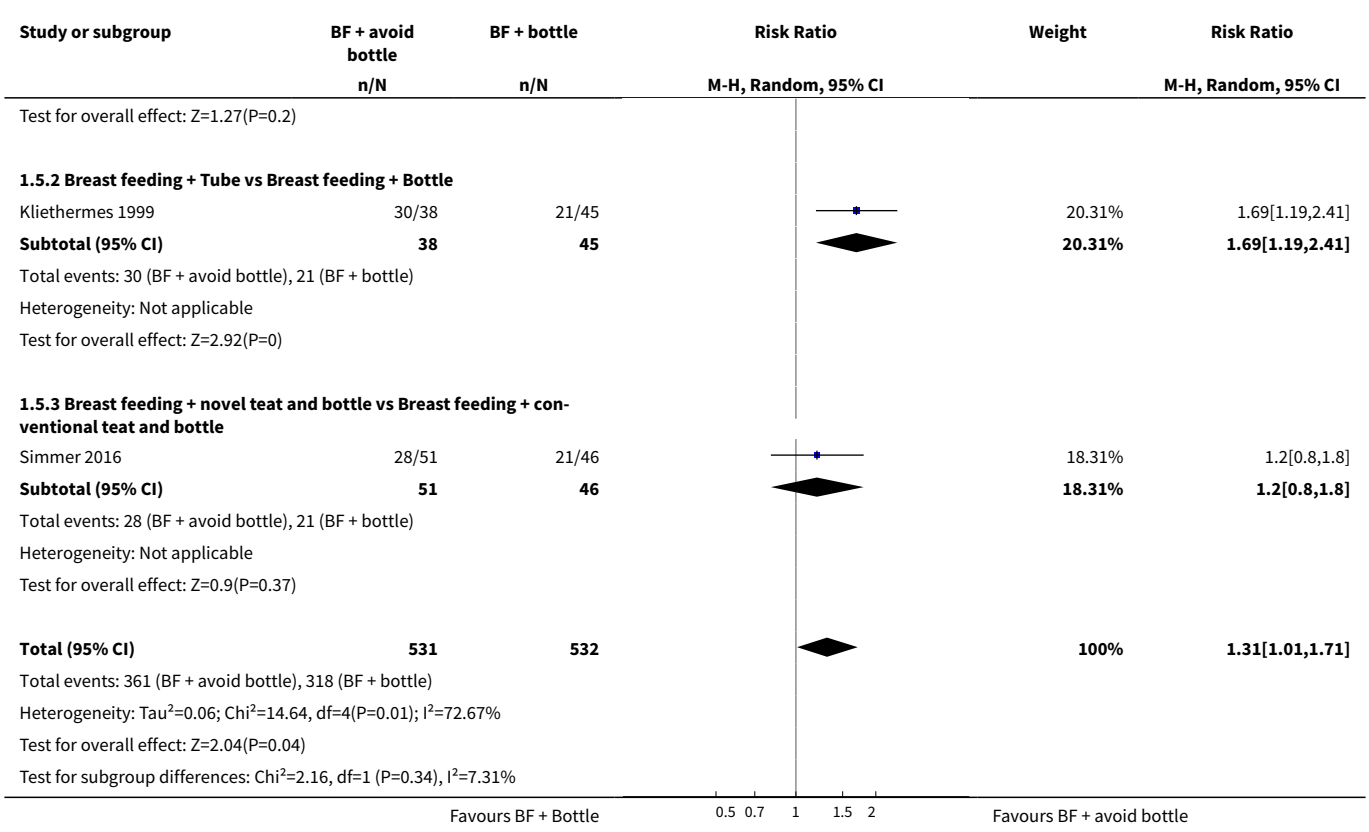
Study or subgroup	BF + avoid bottle n/N	BF + bottle n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 Breast feeding + Cup vs Breast feeding + Bottle					
Collins 2004	112/151	103/152		22.88%	1.09[0.95,1.26]
Gilks 2004	14/27	12/27		2.67%	1.17[0.67,2.04]
Rocha 2002	36/44	27/34		6.79%	1.03[0.83,1.28]
Yilmaz 2014	252/254	244/268		52.93%	1.09[1.05,1.13]
Subtotal (95% CI)	**476**	**481**		**85.28%**	**1.09[1.03,1.15]**
Total events: 414 (BF + avoid bottle), 386 (BF + bottle)					
Heterogeneity: Tau^2=0; Chi^2=0.31, df=3(P=0.96); I^2=0%					
Test for overall effect: Z=3.19(P=0)					
1.4.2 Breast feeding + Tube vs Breast feeding + Bottle					
Kliethermes 1999	34/38	30/46		6.05%	1.37[1.08,1.74]
Subtotal (95% CI)	**38**	**46**		**6.05%**	**1.37[1.08,1.74]**
Total events: 34 (BF + avoid bottle), 30 (BF + bottle)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.61(P=0.01)					
1.4.3 Breast feeding + novel teat and bottle vs Breast feeding + conventional teat and bottle					
Simmer 2016	46/51	37/46		8.67%	1.12[0.95,1.33]
Subtotal (95% CI)	**51**	**46**		**8.67%**	**1.12[0.95,1.33]**
Total events: 46 (BF + avoid bottle), 37 (BF + bottle)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.33(P=0.18)					
Total (95% CI)	**565**	**573**		**100%**	**1.11[1.06,1.16]**
Total events: 494 (BF + avoid bottle), 453 (BF + bottle)					
Heterogeneity: Tau^2=0; Chi^2=4.34, df=5(P=0.5); I^2=0%					
Test for overall effect: Z=4.11(P<0.0001)					
Test for subgroup differences: Chi^2=3.52, df=1 (P=0.17), I^2=43.13%					



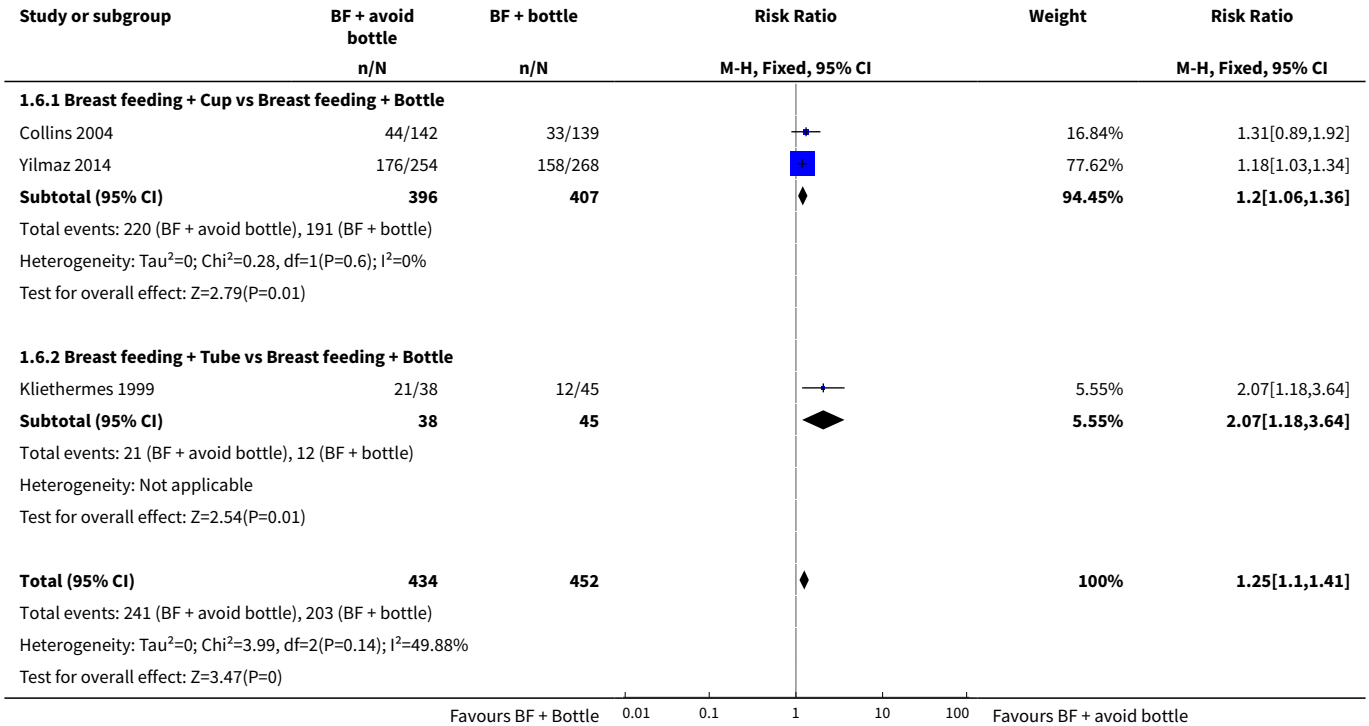
Analysis 1.5. Comparison 1 Breast feeding with supplemental feeds by other than bottle versus breast feeding with supplemental feeds by bottle (all trials), Outcome 5 Any breast feeding at 3 months post discharge.

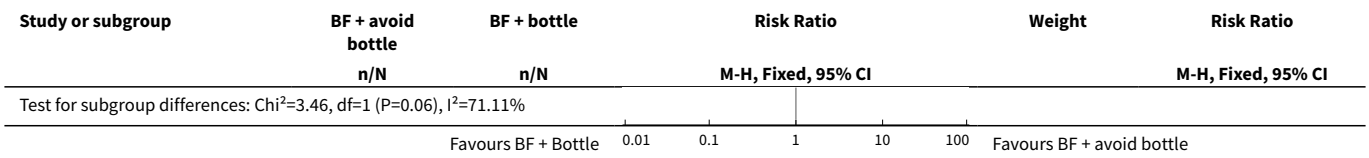
Study or subgroup	BF + avoid bottle n/N	BF + bottle n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.5.1 Breast feeding + Cup vs Breast feeding + Bottle					
Collins 2004	61/144	50/139		22.97%	1.18[0.88,1.58]
Rocha 2002	19/44	5/34		6.97%	2.94[1.22,7.06]
Yilmaz 2014	223/254	221/268		31.44%	1.06[0.99,1.14]
Subtotal (95% CI)	**442**	**441**		**61.38%**	**1.24[0.89,1.71]**
Total events: 303 (BF + avoid bottle), 276 (BF + bottle)					
Heterogeneity: Tau^2=0.05; Chi^2=6.93, df=2(P=0.03); I^2=71.15%					



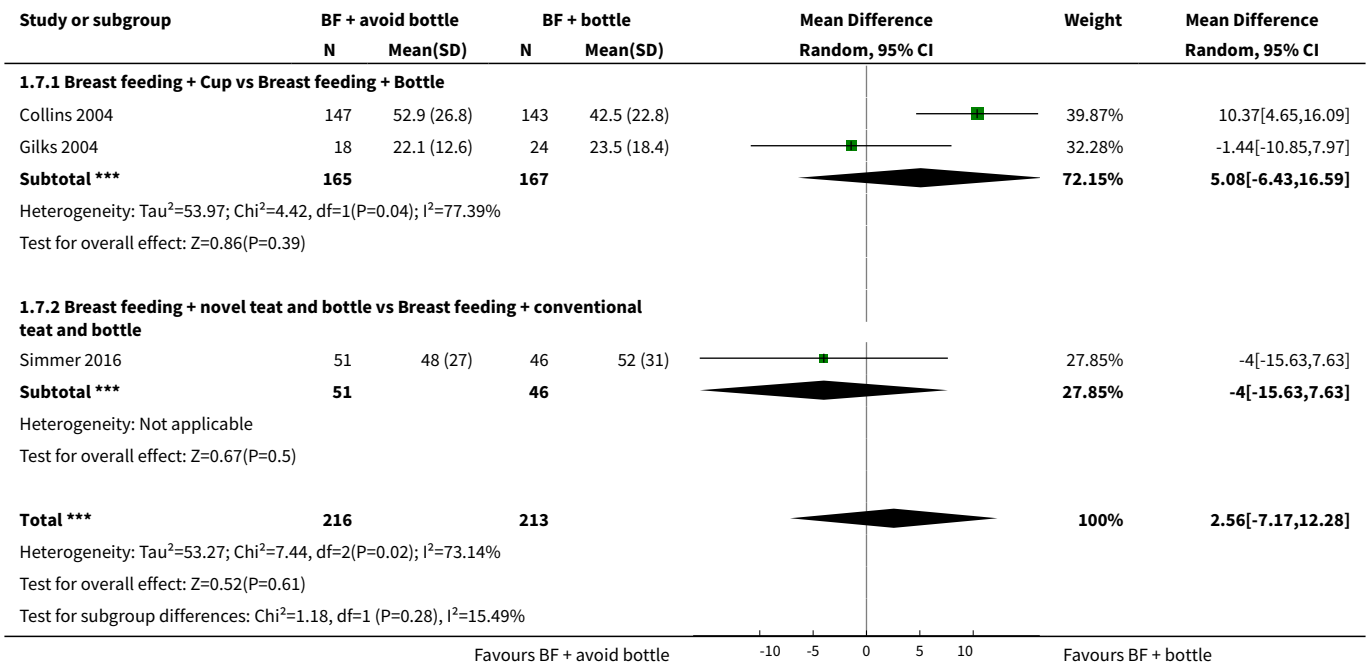


Analysis 1.6. Comparison 1 Breast feeding with supplemental feeds by other than bottle versus breast feeding with supplemental feeds by bottle (all trials), Outcome 6 Any breast feeding at 6 months post discharge.

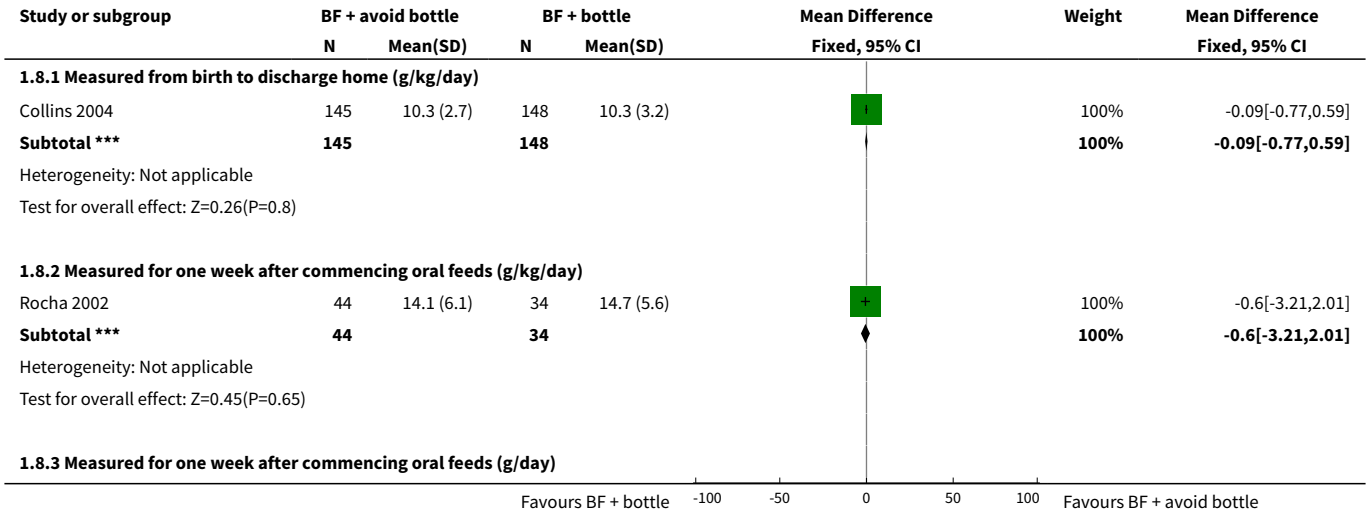


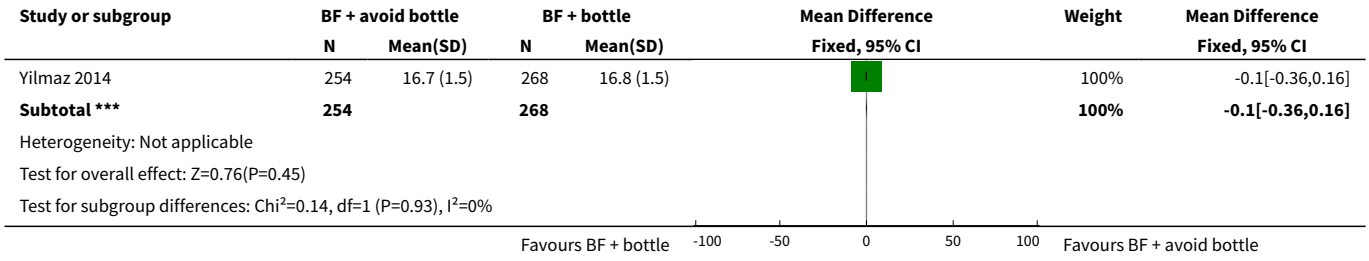


Analysis 1.7. Comparison 1 Breast feeding with supplemental feeds by other than bottle versus breast feeding with supplemental feeds by bottle (all trials), Outcome 7 Days to reach full sucking feeds.

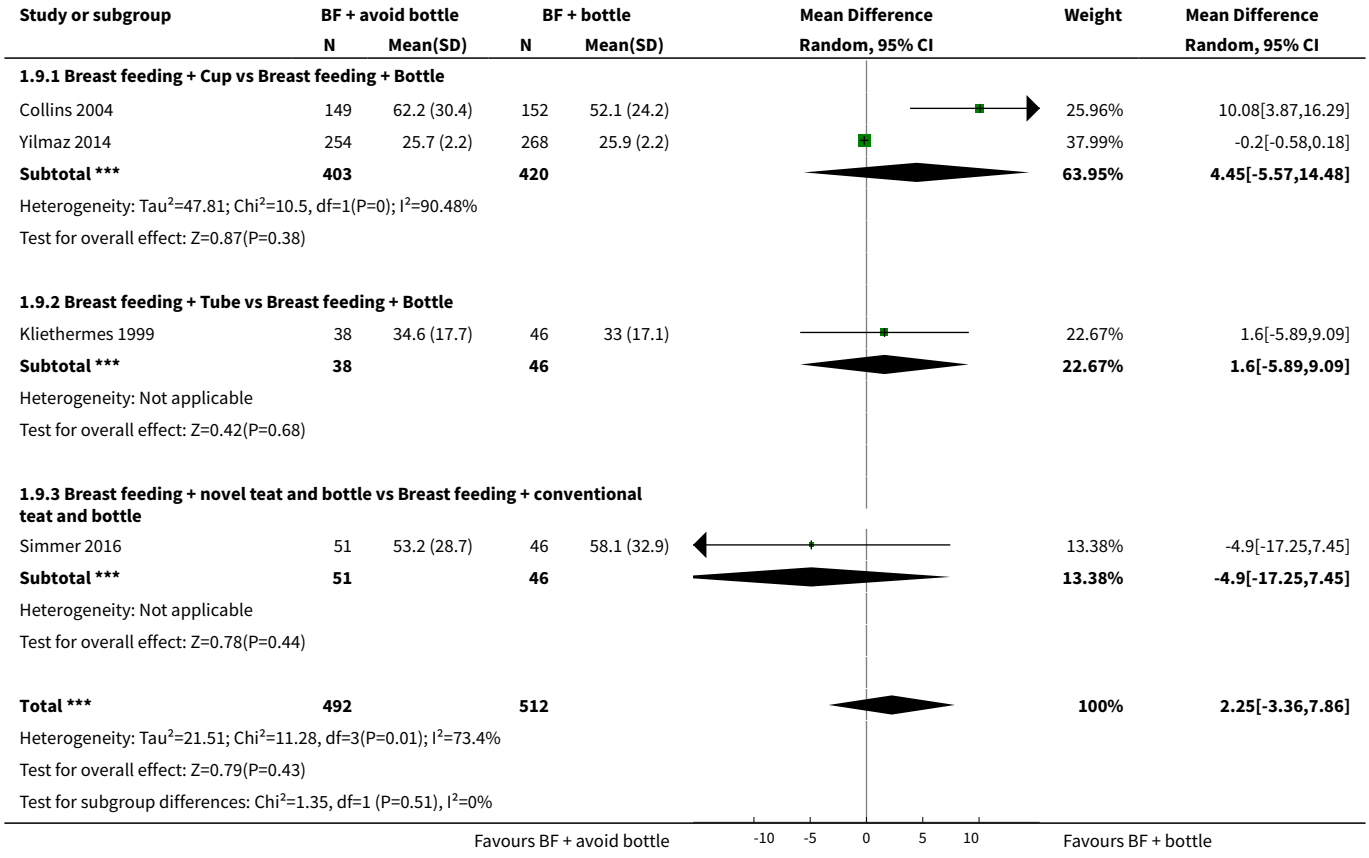


Analysis 1.8. Comparison 1 Breast feeding with supplemental feeds by other than bottle versus breast feeding with supplemental feeds by bottle (all trials), Outcome 8 Weight gain.

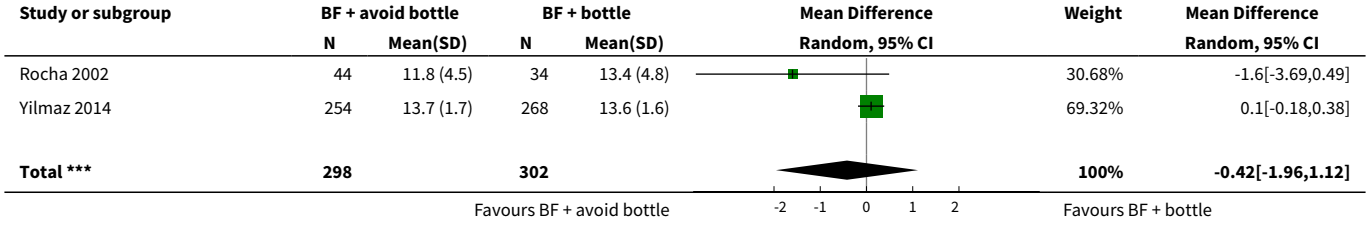


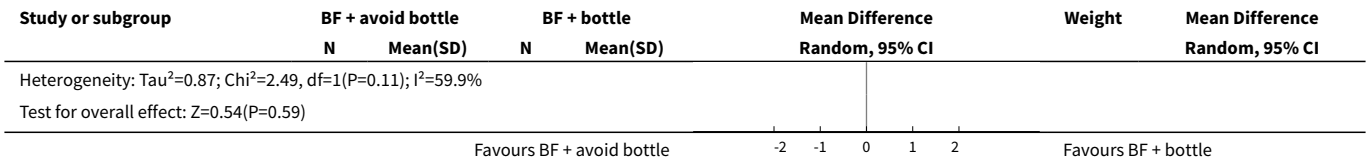


Analysis 1.9. Comparison 1 Breast feeding with supplemental feeds by other than bottle versus breast feeding with supplemental feeds by bottle (all trials), Outcome 9 Length of hospital stay.

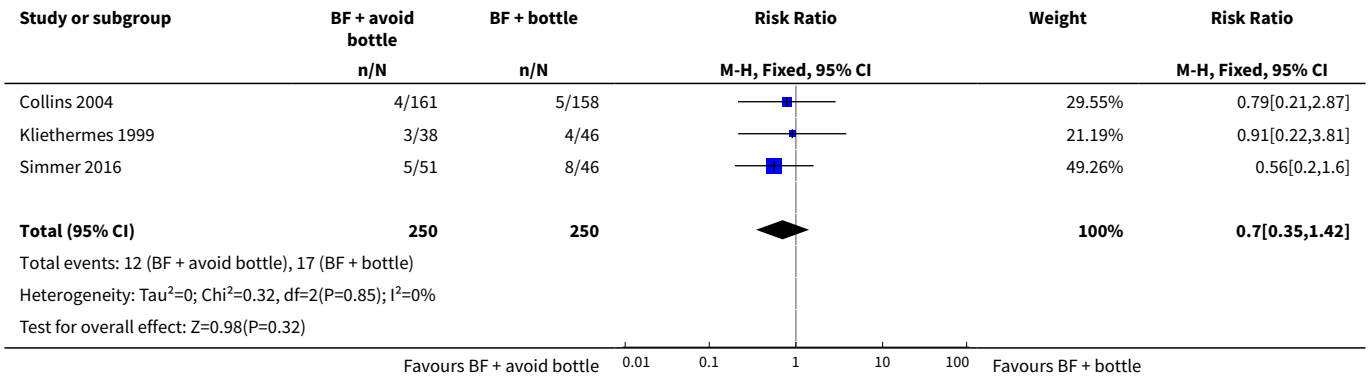


Analysis 1.10. Comparison 1 Breast feeding with supplemental feeds by other than bottle versus breast feeding with supplemental feeds by bottle (all trials), Outcome 10 Duration of supplementary feed.





Analysis 1.11. Comparison 1 Breast feeding with supplemental feeds by other than bottle versus breast feeding with supplemental feeds by bottle (all trials), Outcome 11 Episodes of infection.



APPENDICES

Appendix 1. Standard search methods

PubMed: ((infant, newborn[MeSH] OR newborn OR neonate OR neonatal OR premature OR low birth weight OR VLBW OR LBW or infan* or neonat*) AND (randomized controlled trial [pt] OR controlled clinical trial [pt] OR Clinical Trial[ptyp] OR randomized [tiab] OR placebo [tiab] OR clinical trials as topic [mesh: noexp] OR randomly [tiab] OR trial [ti]) NOT (animals [mh] NOT humans [mh]))

Embase: (infant, newborn or newborn or neonate or neonatal or premature or very low birth weight or low birth weight or VLBW or LBW or Newborn or infan* or neonat*) AND (human not animal) AND (randomized controlled trial or controlled clinical trial or randomized or placebo or clinical trials as topic or randomly or trial or clinical trial)

CINAHL: (infant, newborn OR newborn OR neonate OR neonatal OR premature OR low birth weight OR VLBW OR LBW or Newborn or infan* or neonat*) AND (randomized controlled trial OR controlled clinical trial OR randomized OR placebo OR clinical trials as topic OR randomly OR trial OR PT clinical trial)

The Cochrane Library: (infant or newborn or neonate or neonatal or premature or very low birth weight or low birth weight or VLBW or LBW)

Appendix 2. Risk of bias tool

1. Selection bias (random sequence generation and allocation concealment)

For each included trial, we planned to categorise the risk of selection bias as:

1a. Random sequence generation

1. Low risk: Investigators describe a random component in the sequence generation process, such as referring to a random number table, using a computer random number generator, tossing a coin, shuffling cards or envelopes, throwing dice, drawing lots or conducting minimisation.
2. High risk: Investigators describe a non-random component in the sequence generation process (sequence generated by odd or even date of birth, sequence generated by some rule based on date or day of admission, sequence generated by some rule based on hospital or clinic record number, allocation by judgement of the clinician, allocation by preference of the participant, allocation based on results of a laboratory test or a series of tests or allocation by availability of the intervention).

3. Unclear risk: No or unclear information is provided.

1b. Allocation concealment

For each included trial, we planned to categorise the risk of bias regarding allocation concealment as:

1. Low risk: Participant and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomisation), sequentially numbered drug containers or identical appearance or sequentially numbered sealed opaque envelopes.
2. High risk: Participant and investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on open random allocation schedule (e.g. a list of random numbers), unsealed or non-opaque envelopes, alternation or rotation, date of birth or case record number.
3. Unclear risk: No or unclear information is provided.

2. Blinding (performance bias)

For each included trial, we planned to categorise the methods used to blind study personnel from knowledge of which intervention a participant received.

1. Low risk: no blinding or incomplete blinding, but review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured; unlikely that blinding could have been broken.
2. High risk: no blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; blinding of key trial participants and personnel attempted, but likely that blinding could have been broken, and the outcome is likely to be influenced by lack of blinding.
3. Unclear risk: No or unclear information is provided.

3. Blinding (detection bias)

For each included trial, we planned to categorise the methods used to blind outcome assessors from knowledge of which intervention a participant received.

1. Low risk: no blinding or incomplete blinding, but review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured; unlikely that blinding could have been broken.
2. High risk: no blinding of outcome assessment, but review authors judge that outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment; likely that the blinding could have been broken, and outcome measurement is likely to be influenced by lack of blinding.
3. Unclear risk: No or unclear information is provided.

4. Incomplete outcome data (attrition bias)

For each included trial and for each outcome, we planned to describe the completeness of data including attrition and exclusions from the analysis.

1. Low risk:
   a. No missing outcome data.
   b. Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias).
   c. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
   d. For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk is not enough to have a clinically relevant impact on the intervention effect estimate.
   e. For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes is not enough to have a clinically relevant impact on observed effect size.
   f. Missing data have been imputed by appropriate methods.
2. High risk:
   a. Reasons for missing outcome data likely to be related to true outcome, with imbalance in numbers or reasons for missing data across intervention groups.
   b. For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk is enough to induce clinically relevant bias in intervention effect estimate.
   c. For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes is enough to induce clinically relevant bias in observed effect size.
   d. "As-treated" analysis done with substantial departure of the intervention received from that assigned at randomization.
   e. Potentially inappropriate application of simple imputation.
3. Unclear risk: No or unclear information is provided.

5. Selective reporting (reporting bias)

For each included trial, we planned to describe how we investigated the risk of selective outcome reporting bias and what we found. We planned to access all protocols of the included trials through a search of clinical trials registries (clinicaltrials.gov; controlled-trials.com; and who.int/ictrp) and by direct contact with trial authors.

We planned to assess the methods as follows.

- Low risk: The study protocol is available, and all of the trial's prespecified (primary and secondary) outcomes of interest in the review have been reported in the prespecified way; or the study protocol is not available, but it is clear that published reports include all expected outcomes, including those that were prespecified (convincing text of this nature may be uncommon).
- High risk: Not all of the trial's prespecified primary outcomes have been reported; one or more primary outcomes are reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not prespecified; one or more reported primary outcomes were not prespecified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a trial.
- Unclear risk: No or unclear information is provided (the study protocol is not available).

6. Other potential sources of bias (other bias)

For each included trial, we planned to describe any important concerns that we had about other possible sources of bias (e.g. whether a potential source of bias is related to the specific study design used).

We planned to assess whether each trial was free of other problems that could put it at risk of bias as follows.

1. Low risk: The trial appears to be free of other sources of bias.
2. High risk: The trial has at least one important risk of bias (e.g. the trial had a potential source of bias related to the specific study design used or has been claimed to have been fraudulent or had some other problem).
3. Unclear risk: Risk of bias may be present, but information is insufficient for assessment of whether an important risk of bias exists, or rationale or evidence is insufficient to suggest that an identified problem will introduce bias.

WHAT'S NEW

Date	Event	Description
6 February 2017	Amended	Added external source of support.

HISTORY

Protocol first published: Issue 2, 2005
Review first published: Issue 4, 2008

Date	Event	Description
6 October 2016	Amended	Author reinstated
6 October 2016	New citation required but conclusions have not changed	Author reinstated
24 August 2016	New search has been performed	New searches conducted in July 2016 identified 2 new trials for inclusion. We added 'Summary of findings' tables.
24 August 2016	New citation required and conclusions have changed	Addition of 2 new trials changed the conclusions regarding benefits of breast feeding. We added infection as an outcome.

CONTRIBUTIONS OF AUTHORS

CT Collins wrote the protocol, searched for studies, extracted data, analysed data and wrote the review.
J Gillis contributed to the protocol, extracted data and commented on drafts of the review.
AJ McPhee contributed to the protocol and commented on drafts of the review.
H Suganuma extracted data and commented on drafts of the review.
M Makrides contributed to the protocol and commented on drafts of the review.

DECLARATIONS OF INTEREST

CT Collins and AJ McPhee were investigators responsible for one of the studies included in this review (Collins 2004). J Gillis is a clinical nurse in the Special Care Baby Unit, where one of the included studies was undertaken (Collins 2004).

SOURCES OF SUPPORT

Internal sources

- South Australian Health and Medical Research Institute, Adelaide, South Australia, Australia.
- Neonatal Medicine and Special Care Baby Unit, Women's and Children's Hospital, North Adelaide, South Australia, Australia.
- Salary for Carmel Collins was drawn from an MS McLeod Postdoctoral Research Fellowship (MS McLeod Research Fund, Women's and Children's Hospital Research Foundation), Australia.
- Salary for Maria Makrides was drawn from a National Health and Medical Research Council Principal Research Fellowship (APP1061704), Australia.

External sources

- Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Department of Health and Human Services, USA.

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- National Institute for Health Research, UK.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We added the methods and plan for Summary of findings tables and GRADE recommendations, which were not included in the original protocol.

For the 2016 review, we added infection events as an outcome.

INDEX TERMS

Medical Subject Headings (MeSH)

*Breast Feeding; *Cooking and Eating Utensils; *Infant Formula; *Infant, Premature; Bottle Feeding [*statistics & numerical data]; Enteral Nutrition [methods]; Length of Stay; Milk, Human; Randomized Controlled Trials as Topic; Sucking Behavior

MeSH check words

Female; Humans; Infant, Newborn