Does the use of artificial teats (dummy or bottle) affect breast feeding success in preterm infants? A randomised controlled trial and systematic review.

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Abstract

Establishing successful breast feeding can be difficult for mothers of preterm infants. Artificial teats (dummy or bottle) form part of standard practice in neonatal intensive and special care nurseries but may adversely affect breast feeding outcomes.

This study investigated the relationship between artificial teats and breast feeding outcomes in preterm infants by undertaking a multi-centred randomised controlled trial comparing bottles, cups and dummies in preterm infants less than 34 weeks gestation at birth, and by conducting a systematic review of randomised controlled trials of artificial teats and breast feeding outcomes in preterm infants.

The results of the randomised controlled trial showed that using a dummy had no significant effect on the proportion of infants breast feeding on discharge home (Fully breast feeding versus partially and not: OR 0.84, 95% CI 0.51 to 1.39, P=0.50; Any breast feeding versus not: OR 0.83, 95% CI 0.45 to 1.50, P=0.53). The addition of data from the randomised controlled trial to an existing Cochrane systematic review showed that dummy use did not affect length of hospital stay (weighted mean difference –3.97 days, 95% CI -- 8.10 to 0.15). There appear to be no disadvantages to using a dummy during hospitalisation for the preterm infant.

The results of the randomised controlled trial showed that the use of cups significantly increased the proportion of infants discharged home fully breast feeding (OR 1.73, 95% CI 1.04 to 2.88, P=0.03) but had no significant effect on any breast feeding (OR 1.37, 95% CI 0.78 to 2.38, P=0.27). The use of cups significantly increased the risk for an increased time to reach all sucking feeds (HR 1.75, 95% CI 1.34 to 2.28, P<0.001) and increased length of hospital stay (HR 1.41, 95% CI 1.09 to 1.82, P=0.01).

The results of the systematic review showed that avoiding the use of a bottle during the transition to breast feeds has significant advantages for breast feeding success on discharge home (Fully: RR 1.41, 95% CI 1.19 to 1.69; Any: RR 1.13, 95% CI 1.01 to 1.2) and at three and six months post discharge. However more research is needed on the method of 'no bottle'. There do not appear to be any negative effects of a tube alone approach in the transition to breast feeds, but there is a non significant increase in any breast feeding and a longer duration of time to full sucking feeds and length of stay with cup feeds.

Declaration

This work contains no material which has been accepted for the award of any other degree of diploma in any university and that, to the best of my knowledge and belief, the thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

I give consent to this copy of my thesis, when deposited in the University library, being available for loan and photocopying.

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Abbreviations

CI	Confidence interval
CPAP	Continuous Positive Airway Pressure
FG	French gauge
HMD	Hyaline Membrane Disease
HR	Hazard ratio
IPPV	Intermittent Positive Pressure Ventilation
MD	Mean Difference
MHW	Mercy Hospital for Women
NICU	Neonatal Intensive Care Unit
NNS	Non nutritive sucking
NNT	Number needed to treat
OR	Odds ratio
PPHN	Persistent Pulmonary Hypertension
PV/IVH	Periventricular/intraventricular haemorrhage
PVLE	Periventricular leucoencephalopathy. Periventricular cyst formation in the white matter of preterm infants
RD	Risk difference
RR	Relative risk
SE	Standard Error
SD	Standard Deviation
WCH	Women's & Children's Hospital
WMD	Weighted mean difference

Glossary

APNOEA. Recurrent pauses in breathing of more than 20 seconds or for less than 20 seconds associated with bradycardia or desaturation requiring intervention.

COMPLEMENTAL FEED. Giving extra expressed breast milk or formula after a breast feed.

'NON SPECIFIC' RESPIRATORY DIAGNOSIS. Any non specific respiratory distress in term and preterm infants requiring support (combines transient tachypnoea and immature lung).

NORMAL RESPIRATORY DIAGNOSIS. Normal lungs. No respiratory disease and no respiratory support.

SUPPLEMENTAL FEED. Replacement of a breast feed with expressed breast milk or formula.

Chapter 1. Introduction

Breast milk is the feed of choice for preterm infants because of its significant nutritional and non nutritional benefits. The benefits of breast milk include increased protection against infection, improved feed tolerance, and improved neurological outcome and protection against allergies (Gross and Slagle 1993; Schanler et al. 1999). In addition, it may confer a psychological benefit on the mother from the contribution to the care of her baby in such a positive way.

Establishing breast feeding can be difficult for mothers of preterm infants. The majority of mothers choose to breast feed their preterm infants, yet there is a substantial decrease in the number discharged home from hospital breast feeding. Clinical practices within the neonatal intensive and special care environments require evaluation of the impact they have on breast feeding, to ensure no harm is caused. The use of artificial teats (dummy or bottle) is the practice under review for this thesis.

It is standard practice to give preterm infants dummies, however the effect that dummies have on subsequent breast feeding outcomes is unknown in this population.

The process for establishing breast feeding in preterm infants differs markedly from term infants. Preterm infants who are unable to suck are fed by a gavage tube until they are mature enough to commence the transition to breast feeds. When this occurs and the infant can tolerate sucking feeds, it is often difficult for mothers who choose to breast feed their preterm infant to always be present for a breast feed. The conventional practice is to use a bottle when the mother is unable to be present to breast feed. There is, however, controversy over the use of bottles for complementing and supplementing breast feeds and cup feeding has been suggested to increase the likelihood of establishing successful breast feeding (Lang et al. 1994).

In 1995, at the time this research was designed and commenced, there were no randomised controlled trials of interventions to support the preterm infant's transition to breast feeds. There was little information on the physiological effects of cup feeding on term or preterm infants. Observational studies showed that dummies were associated with shorter breast feeding duration in term infants. This research was therefore based on the evidence available at that time. Since 1995 advances in knowledge have occurred especially in the

term infant population (Schubiger et al. 1997; Kramer et al. 2001a; Kramer et al. 2001b; Howard et al. 2003). There has been one randomised controlled trial (Rocha et al. 2002) and one pilot study (Mosley et al. 2001) of the use of cup feeding in relation to breast feeding outcomes in preterm infants.

This study aims to investigate the relationship between artificial teats and breast feeding outcomes in preterm infants:

- by undertaking a randomised controlled trial comparing bottles, cups and dummies in preterm infants less than 34 weeks gestation at birth, and
- by conducting a systematic review of randomised controlled trials on this topic.

The principal research hypotheses for the randomised controlled trial are:

1. *That preterm infants who have non nutritive sucking on a dummy have a different breast feeding success rate from preterm infants who do not have dummy sucking opportunities.*
2. *That a strategy of breast and cup feeding of growing preterm infants results in a different breast feeding success rate from a breast and bottle strategy.*

In Chapter Two the context for the study is set with a review of the literature highlighting current evidence on the use of dummies, interventions in the transition to breast feeds and the current state of knowledge of cup feeding in both the preterm and term population. In Chapter Three, the research methods used to conduct the randomised controlled trial are detailed, and the baseline data and participant flow are presented in Chapter Four. The findings of the primary study end points are presented in Chapter Five and the secondary study end points in Chapter Six. Exploratory sub group analyses are discussed in Chapter Seven. A discussion and critique of the results from the randomised controlled trial are presented in Chapter Eight. The reporting of the randomised controlled trial follows the guidelines of the revised CONSORT statement for reporting randomised controlled trials (Altman et al. 2001). The protocols for the conduct of two systematic reviews are presented in Chapter Nine and the results in Chapter Ten. One systematic review reports the addition of data from the randomised controlled trial reported in this thesis to an existing review on the effect of the use of dummies on preterm infants, and the other compares the use of no bottles to bottles in the transition to breast feeds for preterm infants. The conduct and the reporting of the systematic reviews follows the standard format of the Cochrane Collaboration as described in the Cochrane Reviewer's Handbook

(Clarke et al. 2003) and the Neonatal Collaborative Review Group (Sinclair et al. 2003). Conclusions are presented in Chapter Eleven.

Chapter 2. Background and Literature review

2.1 Scope

The need for the research and the research design was based on the evidence available when the study was designed in 1995. Knowledge in this area has developed since that time and these advances are incorporated in the literature review.

Computerised searches were conducted using MEDLINE (1966 to May week three 2003), CINAHL (1982 to May week three, 2003), Cochrane Central Register of Controlled Trials register (Issue 2, 2003) and EMBASE (1980 to Week 21 2003). MESH headings included the following: Breast feeding, Milk, human, Infant, Preterm, Infant, Low birth weight, Infant, Very low birth weight, Infant, Newborn, Infant feeding supplemental, Infant equipment, Bottle feeding. The following text words were used: Pacifier, Dumm$, Cup, Cup Feed$, Cupfeed$, Non, Nutritive, Sucking.

2.2 Transition from tube to breast feeds in preterm infants

Preterm infants (defined as less than 37 completed weeks gestation at birth) commence sucking feeds when they are mature enough to coordinate a suck swallow breath pattern. This was generally accepted to occur at around 32 to 34 weeks gestation (Lemons and Lemons 1996). It has since been shown that preterm infants are capable of nutritive sucking at the breast (defined as the ingestion of at least five millilitres of milk) from as early as 30 ½ weeks (Nyqvist et al. 1999; Nyqvist et al. 2001).

Before commencing sucking feeds, milk feeds are given via a nasogastric or orogastric tube, the amount and frequency dependent on gestational age. The number of sucking feeds is increased gradually, usually beginning with one a day and increasing as the baby demands or is assessed to be ready to progress. As the number of sucking feeds increases the number of tube feeds decreases until the baby is taking all sucking feeds.

It is often difficult for mothers to be with their baby for all breast feeds once the frequency of sucking feeds increases. When she is unavailable, the conventional practice is for the mother's milk to be given by bottle. It is also common practice during the early stages of breast feeding for infants to be complemented or 'topped up' after a breast feed either by

bottle or by gavage tube, using expressed breast milk or artificial milk. Dummy use is also encouraged for all preterm infants.

2.3 Breast feeding prevalence in preterm infants.

Establishing breast feeds can be difficult for a mother and her preterm baby. Unpublished data (1990-1994) from the Women's and Children's Hospital (WCH), Adelaide, showed that the majority of mothers (79%, n=763/966) whose infants were less than 34 weeks gestational age at birth chose to express breast milk for their baby[1]. On discharge home from the WCH this had fallen to 45% (n=178/396) who were fully breast feeding and 59% (n=234/396) any breast feeding[2]. Approximately 10% of women stopped expressing before their baby commenced breast feeds, the remainder stopped during the transition time.

There are few published reports of preterm infants' breast feeding outcomes in Australian neonatal units. It is difficult to make comparisons between studies due to differences in reporting of gestational age or birth weight; differing groupings of gestational ages; discharge from the unit or discharge home; partial or exclusive breast feeding. Dawson and Benson (2001) report a 62% exclusive breast feeding rate on discharge from their neonatal intensive care unit (NICU). They audited 405 infants whose mothers wished to breast feed during a 12 month period, approximately half were term and half preterm. Discharge from their unit included infants who were transferred to another hospital (61%) and those who were discharged home (39%). The eventual breast feeding outcomes for those infants transferred to another hospital are not reported.

The proportion of infants breast feeding (partial and exclusive) on discharge home from a Brisbane NICU for infants less than 1500g has been reported as 54% (n=44), and for infants less than 1000g, 33%, (n=7) (Doherty and Sparkman 1997). Of 81 infants less than 33 weeks gestation who received breast milk in an Adelaide NICU, 62% were discharged home still receiving some breast milk (Simmer et al. 1997). In an audit undertaken of all infants less than 35 weeks admitted to a Sydney NICU during a 12 month period (n=155), 83% had received breast milk (Yip et al. 1996). By time of discharge home this had dropped to 64% having some breast milk (45% exclusive and 19% partial).

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[1] Excludes infants who died (n=103).

[2] Excludes infants transferred to peripheral hospitals before discharge home (n=570).

The breast feeding prevalence for term infants, in comparison, is higher. Donath and Amir (2000) analysed data from the 1995 Australian National Health Survey involving 3,252 children under the age of four years. They showed that 81.8% of infants were discharged home breast feeding, by three months 62.6% were breast fed (57.1% exclusively) and by six months 46.2% (18.6% exclusively).

These data highlight the difficulty in establishing breast feeding in mothers of preterm infants. The substantial decrease from those choosing to express milk for their baby to those who go home breast feeding is of concern.

2.4 Preterm infants ability to breast feed

In clinical practice breast feeding was commonly thought to be more stressful than bottle feeding, however this has not been substantiated by research (Meier 1988). Meier measured the responses of five preterm infants less than 1500g to bottle and breast feeding. The infants served as their own controls; 71 feeding sessions were studied (Meier and Anderson 1987; Meier 1988). Transcutaneous oxygen levels differed during bottle and breast feeding with a greater decline during bottle feeding, which persisted after the feed. Infants showed better coordination of sucking, swallowing and breathing during breast feeding. The mean duration of breast feeds, however, was significantly greater than bottle feeds.

Meier conducted a second study, again of preterm infants less than 1500g (Meier et al. 1991). Mean oxygen saturation was consistently higher during breast feeding than bottle feeding. Further studies have confirmed these results (Bier et al. 1993; Young 1995; Bier et al. 1997; Chen et al. 2000), to show that when bottle feeding it is more difficult for the preterm infant to coordinate sucking, swallowing and breathing than when breast feeding.

2.5 Sucking action during breast feeding

The use of real time ultrasound imaging has enabled the breast feeding process in the term infant to be visualised (Woolridge 1986). A sucking or 'stripping' action occurs in the following sequence:

- The nipple and much of the areola is drawn into the mouth, the lacteal sinuses being drawn into the mouth with the breast tissue, filling the oral cavity, the nipple extending

to the junction of the hard and soft palate. The tongue is cupped around the nipple and is well forward covering the lower gum.

- The tongue moves in a roller like peristaltic wave from front to back, which squeezes milk from the nipple (at the same time the lower jaw rises and constricts the lactiferous sinuses.) This positive pressure is the primary force in removing milk.
- The baby swallows, with the cycle of compression ending at the posterior base of the tongue.
- Depression of the back portion of the tongue creates a negative pressure that draws the nipple once more into the mouth, accompanied by a lowering of the jaw allowing milk to flow back into the lactiferous sinuses (Woolridge 1986).

The only study to use other than direct observation to describe preterm infant sucking behaviour during breast feeding was published in 2001 (Nyqvist et al. 2001). Twenty-six infants were investigated during breast feeding using electromyography. At the time of the study the infants were at 32.1 to 37.1 postmenstrual weeks (calculated from the number of weeks since the mother's last menstrual period). These infants showed evidence of early sucking competence with wide individual variations, unexplained by maturational level or postnatal age. Sucking time made up 39% of the total time, mouthing 10% and pauses 22%. A higher duration of sucks was found in older infants, which may indicate a higher level of milk intake.

There have been no published studies using ultrasonography in the preterm population.

2.6 Sucking action during bottle feeding

Real time ultrasound imaging has been conducted on term and preterm infants bottle feeding (Bu'Lock et al. 1990). The tongue does not extend as far anteriorly as it does in a breast feeding baby, the bottle teat does not penetrate as deeply as the breast, and recoils in a vertical plane – unlike the breast which is maintained in a moderate state of compression (Bu'Lock et al. 1990). Bu'Lock et al. (1990) found the tongue action to be otherwise the same as for a breast fed baby, with a peristaltic, wave like action anterio -posteriorly. This contrasts with Riordan (1998) who describes the tongue action as being piston like, with the tongue thrust forward against the end of the teat to control the milk flow. Riordan (1998) also describes the difference in the mouth position for bottle feeding, the lips being

held closer together than for breast feeding, and pursed to maintain contact with the teat (Riordan 1998).

In Bu'Lock et al's (1990) study five term, four 35 to 36 weeks gestation and five 33 to 34 weeks gestation infants were scanned during bottle feeding. The term infants were studied at day four postpartum with the reason given that 'normal' feeding takes three to four days to establish. It would have been useful to study the infants progressively from birth to see if greater differences were present in the early feedings, and if the observed difference by day four was one of adjustment to the artificial teat.

The preterm infants were studied from 4 to 19 days after birth. The lower the gestational maturity, the more poorly coordinated were the tongue movements. Tongue movements ranged from incomplete or fragmentary peristaltic waves, flickering or writhing movements to twitching or tremulous movements, to closing off the end of the teat using the tip or distal portion of the tongue. Term infants synchronise the coordination of sucking, swallowing and breathing in a ratio of 1:1:1 during feeding. To protect their airway the more preterm infants alternated periods of apnoea when feeding with periods of breathing, and by blocking the end of the teat with their tongue. Their success in protecting the airway in this manner is indicated by the absence of external evidence of feeding difficulties – gagging or distress. The small number of preterm infants in this study precludes generalisation. The authors however postulate that these alternate ways of keeping the airway open during feeding could become habitual, their origin due to adverse early experiences, for example, breathing difficulties during feeding.

Inoue et al. (1995) suggest that the role of the jaw motion has not been studied sufficiently. As ultrasonography can only view a narrow field, the observations have been focused on the motion of the tongue only. They suggest the tongue alone is insufficient for milk ingestion and the jaw plays a significant part. They have used electromyography to show significant differences between breast and bottle fed infants' masseter muscle activity during feeding. The amount of masseter muscle work for a breast feeding baby is significantly more than for bottle feeding.

2.7 Sucking action during dummy use (non nutritive sucking)

Non nutritive sucking refers to sucking without oral fluid intake as occurs when using a dummy. The pattern of non nutritive sucking differs from nutritive sucking and is characterised by bursts of rapid sucks followed by pauses and is present as early as 26 weeks gestation in preterm infants (Daniels et al. 1986; Hafstrom and Kjellmer 2000; Hafstrom and Kjellmer 2001). During nutritive sucking, the sucking bursts are longer than the sucking pauses, whereas in non nutritive sucking there are longer sucking pauses and a faster sucking rate (Daniels et al. 1986). Bu'Lock et al. (1990) also used ultrasonography to study infants during a period of non nutritive sucking. Tongue movements were similar between nutritive and non nutritive sucking and swallowing was rarely observed during non nutritive sucking.

2.8 Why artificial teats are thought to interfere with breast feeding.

The term *nipple confusion* has been used in the literature since the early 1980's (Marmet and Shell 1984) to describe the clinical observation that using an artificial teat (dummy or bottle) can interfere with an infant's ability to breast feed. It is a widely used term, one that is commonly promoted in consumer based literature (Neifert et al. 1995). However, there is not an agreed or formal definition for nipple confusion and the existence of the phenomenon is the subject of debate (Fisher and Inch 1996; Hunter 1997). Its existence is based on anecdotal observation; the mechanical or physiological basis, incidence and necessary maternal and infant factors have not been established (Neifert et al. 1995).

Supporters of the existence of the phenomenon use the term to describe situations where an infant has an artificial teat, subsequent to which breast feeding difficulty is experienced (breast feeding may or may not have been successful prior to the artificial teat) (Neifert et al. 1995). Neifert et al. (1995) have proposed four hypotheses to explain the mechanism of nipple confusion:

- That sucking on an artificial teat interferes with the physiologic action of normal breast feeding, with the infant adjusting to a sucking pattern that compresses and controls the teat, including the adaptation to control volume and fluid flow.
- That a baby "imprints" to the first feed; if this is an artificial teat it will make attempts at breast feeds more difficult.

- The low volume of colostrum associated with breast feeding in the first few days compared with large volume available from a bottle may accustom the infant to higher volumes, making breast feeding attempts more difficult.
- Infants already experiencing difficulty with initial attempts at breast feeding are more likely to be given bottles, rewarded by the availability of milk and therefore perceive bottle feeding as easier.

The association of bottle feeding with difficulty in breast feeding is not a recent observation. In 1948 Davis referred to the *'well recognised clinical observation'* (p556) of the difficulty in successfully breast feeding a baby that has been started on bottle feeds (Davis et al. 1948).

2.9 Dummy use

2.9.1 Effect on breast feeding in term infants

Several large observational studies have shown a significant relationship between dummy use and early weaning in term infants (Victora et al. 1993; Ford et al. 1994; Barros et al. 1995; Righard and Alade 1997; Victora et al. 1997; Aarts et al. 1999; Howard et al. 1999b; Vogel et al. 2001). Whether the relationship was causal or not remained unknown. Was dummy use a marker of breast feeding difficulties or of a mother's reduced motivation to continue breast feeding? In contrast, infants who sucked their thumb rather than a dummy showed no relationship with duration of breast feeding (Aarts et al. 1999). Victora et al. (1997) conducted an ethnographic study that suggested that dummy use did not seem to affect those who felt comfortable about breast feeding but contributed to earlier weaning among those who were uncomfortable, thus implying that dummy use may be used as a weaning tool. Aarts et al. (1999) did not find such an association. The mothers in their study intended to breast feed for greater than six months and had breast fed previously for at least four months, however those who used a dummy had a shorter breast feeding duration.

Two randomised controlled trials have studied the effect dummies have on breast feeding outcomes in term infants (Kramer et al. 2001a; Howard et al. 2003) with conflicting results.

Kramer et al. (2001a) conducted a randomised controlled trial on the effect of dummy use on early weaning and cry/fuss behaviour. The study was undertaken in a postnatal ward of a university teaching hospital in Montreal, Canada. Eligibility criteria included the woman's stated intention to breast feed for at least three months, the delivery of a healthy term singleton infant of birth weight greater than 2500g. Two hundred and eighty one mother infant pairs were randomised to receive one of two counselling interventions. For the experimental intervention the mother was asked to avoid dummies when her infant cried or fussed, instead she was advised to offer the breast first, then to try carrying and rocking. In the control group all options were discussed with the mother for calming the infant including breast feeding, carrying, rocking and using a dummy. It is not stated whether bottles were used in either of the groups. The main outcomes were early weaning (within the first three months) and duration of crying, fussing and dummy use at four, six and nine weeks as recorded in twenty four hour infant behaviour logs.

Based on current literature, they calculated that a sample size of 140 in each group would detect a reduction in dummy use from 60% to 40% which would reduce the risk of weaning before the age of three months from 40% to 35% at $P \leq 0.05$ with 90% power. Women were stratified by parity and previous breast feeding experience. The allocation was contained in an opaque envelope, which was opened by a research nurse after consent was obtained. Mothers were asked to complete behaviour diaries on three consecutive days when their infants were four, six and nine weeks of age. Mothers were interviewed at three months by a research assistant blinded to intervention group.

Two hundred and fifty-eight mothers completed the study (127 experimental, 131 control). An intention to treat analysis was undertaken on those who completed the study. The intervention significantly changed dummy use: 38.6% of mothers in the experimental group did not use a dummy compared with 16.0% in the control group, RR 2.4, 95% CI 1.5 to 3.8. Daily use of a dummy was also reduced in the experimental group (40.8% versus 55.7%, RR 0.7, 95% CI 0.6 to 0.95). The mean number of dummy insertions per day at four, six and nine weeks of age was also significantly reduced.

There was no difference in weaning by three months of age between the experimental (18.9%) and the control group (18.3%), RR 1.0, 95% CI 0.6 to 1.7. There was no difference in the cry/fuss behaviour of infants in either group at four, six and nine weeks.

The researchers stated a priori that they would examine differences in results from analyses based on randomised allocation or actual use of dummies to assess the bias occurring with an observational versus experimental design. The observational analysis showed very different results. For exposure based on whether the infant had ever used a dummy (irrespective of study allocation) 21.3% had weaned compared with 11.4% who had never used a dummy (RR 1.9, 95% CI 1.1 to 1.3). The authors suggest that this combination of findings show that dummy use is a marker of breast feeding difficulties or reduced motivation to breast feed rather than the true cause of early weaning. They also detected no beneficial effects of dummy use on infant crying or fussing.

This was the first published randomised controlled trial of the effect of dummy use on breast feeding. Although dummy use was significantly reduced in the experimental group, a substantial proportion (61.4%) still used a dummy compared to 84% in the control group. The authors did not explore the characteristics of the mothers who did not comply with their randomised allocation, there may have been a systematic difference in these women. In addition a larger sample size may have been able to detect a small increased risk of early weaning. Their data on dummy use were based on maternal self report, however that has been the basis for all the observational studies. There was the possibility for selection bias with the research nurse selecting the allocation assignment. Despite the methodological limitations the study provided strong evidence to suggest that dummy use may be a predictor but not a cause of early weaning.

Howard et al. (2003) conducted a randomised controlled trial to evaluate the effects of dummy use and in-hospital cup feeding and bottle feeding on breast feeding in term infants. The study was undertaken in a University affiliated community hospital in the United States of America. Eligibility criteria included women who intended to breast feed, had uncomplicated singleton pregnancies and either wanted their infant to use a dummy or were undecided. Seven hundred women were randomised to one of four interventions: bottle/early dummy, bottle/late dummy, cup/early dummy, cup/late dummy. Supplemental feeds were only given if needed and according to randomised allocation, cup or bottle. The early dummy group were instructed to use the dummy within two – five days, the late dummy group were instructed to avoid using a dummy until the infant's fifth week.

Based on their hospital's breast feeding rates, the researcher's calculated that a sample size of 700 would detect a 10% difference in breast feeding cessation at four weeks postpartum

with P=0.05 and 90% power. The allocation was contained in an opaque envelope. Telephone interviews were conducted at 2, 5, 10, 16, 24, 38 and 52 weeks by a researcher blinded to group assignment. The study investigators, research assistants and nurses conducting the interviews were blinded to group assignment. Data on breast feeding duration were obtained for 686 (98%) and an intention to treat analysis undertaken.

At four weeks postpartum, infants randomised to early dummy (introduced at 2 - 5 days) compared to late dummy (yet to be introduced) showed a significantly reduced prevalence of exclusive breast feeding (OR 1.5, 95% CI 1.0 to 2.0, P=0.03) but did not demonstrate a significant effect on full breast feeding or any (exclusive, full and partial) breast feeding. Early dummy introduction also significantly reduced the duration of any breast feeding. The median number of days for early introduction of a dummy was 140 (95% CI 120-157) and late introduction of dummy was 163 days, (95% CI 140-180), (adjusted hazard ratio (HR) 1.20, 95% CI 1.02 to 1.42, P=0.03).

This study provides strong evidence that early introduction of a dummy can have a detrimental effect on breast feeding in term infants.

Results for the cup and bottle intervention are reported in section 2.10.2.

2.9.2 Use of dummies with preterm infants

The use of dummies in Neonatal and Special Care Units is standard practice, certainly in developed countries. The rationale for their use is that non nutritive sucking helps the development of sucking behaviour, improves digestion and provides comfort and pain relief.

2.9.2.1 Gastro-intestinal effect

Non-nutritive sucking was assessed in relation to tube feeds (before, during or after tube feeding) in ten randomised or quasi randomised trials (Measel and Anderson 1979; Field et al. 1982; Bernbaum et al. 1983; Szabo et al. 1985; De Curtis et al. 1986; Widstrom et al. 1988; Ernst et al. 1989; Sehgal et al. 1990; Kanarek and Shulman 1992; Mattes et al. 1996). These studies aimed to identify the effect of non nutritive sucking on nutritional function and feeding performance by bottle, they were not designed to assess the effect on breast feeding.

Increased weight gain was reported in two trials (Bernbaum et al. 1983; Field and Goldson 1984) but nutrient intake may not have been equal in the groups. In the two trials that controlled for nutrient intake (Ernst et al. 1989; Mattes et al. 1996) no difference in weight gain was found. On meta-analysis there was an overall non significant effect on weight gain (Pinelli and Symington 2003). Based on the current evidence there is no clear benefit of dummy use on weight gain.

A decrease in the number of days to the first oral (bottle) feed (Measel and Anderson 1979; Field et al. 1982) has been reported. Dummy use was also found to reduce the number of days in transition from gavage to full oral (bottle) feeds (Measel and Anderson 1979; Field et al. 1982; Bernbaum et al. 1983; Sehgal et al. 1990). The studies of Measel and Anderson (1979), Field et al. (1982) and Bernbaum et al. (1983) examined the impact of dummy use during tube feeds only. Dummies were allowed for both experimental and control groups outside tube feeding times in three of the studies (Measel and Anderson 1979; Field et al. 1982; Sehgal et al. 1990) and not allowed in the remaining study (Bernbaum et al. 1983). More recently, Mattes et al. (1996) compared the effect of sweetened dummies, latex dummies and maternal heartbeat sounds administered during tube feeds on growth and sucking in preterm infants. They did not report if dummies were used outside tube feeds. They showed no difference in the ages at which the first and total oral (bottle) feeds occurred.

Dummy use, therefore, may shorten the time to full oral feedings. It is difficult to interpret these data with regard to breast feeding. A shorter time to bottle feeds cannot be extrapolated to mean successful breast feeding.

Duration of hospital stay was found to be reduced by approximately six days in the three trials in which this was measured (Measel and Anderson 1979; Field et al. 1982; Bernbaum et al. 1983). Meta-analysis showed a significant reduction in hospital stay (Weighted mean difference (WMD) -7.1 days, 95% CI -12.6 to -1.7) (Pinelli and Symington 2003).

Gastric emptying (Szabo et al. 1985), gastric residual volume (Widstrom et al. 1988) and gastrointestinal transit time (Bernbaum et al. 1983; De Curtis et al. 1986; Ernst et al. 1989) were unaffected by non nutritive sucking.

The effect of dummy use on specific hormones in tube fed infants has been studied (Widstrom et al. 1988; Kanarek and Shulman 1992). Kanarek and Schulman (1992) found that dummy use did not alter blood concentrations of motilin, gastrin, insulin or insulin-like growth factor-1. Widstrom et al. (1988) showed a decreased level of somatostatin with dummy use, the mechanism and importance of this are unclear.

2.9.2.2 Effect of dummies on the behavioural state of preterm infants

The effect of dummies on behavioural state during tube feeds is equivocal. Field et al. (1982) found no effect on behavioural state with dummy sucking during tube feeds. DiPietro et al. (1994) in contrast, reported that preterm infants showed less behavioural distress, spent less time in fussy and active awake states and returned to sleep faster with dummy sucking.

Dummies have a positive effect on behavioural state prior to, and following, bottle feeds (Gill et al. 1988; Gill et al. 1992; McCain 1992; Pickler et al. 1993; McCain 1995; Pickler et al. 1996; Yu and Chen 1999). When using a dummy, infants experienced fewer restless states and more active awake states before feeding, in addition they settled more quickly after the feed than those who did not use a dummy. It is thought that an infant in an alert state is in a more optimal state for feeding than if they were sleeping or distressed (Pickler et al. 1996). When feeding was assessed using the complex feeding scale, Pickler et al. (1993) showed higher feeding performance with dummy use for five minutes pre-feed. In a later study there were no differences in feeding performance with or with out dummy use (Pickler et al. 1996).

2.9.2.3 Pain relief

At the time this research was designed the evidence was not conclusive on the role of dummies in providing pain relief during procedures such as heel prick blood sampling and venepuncture. Field and Goldson (1984) randomly assigned healthy term infants (n=48), preterm infants receiving minimal care (n=48) and preterm infants receiving intensive care (n=48) to receive non nutritive sucking during, and for two minutes following, heel prick blood sampling. They found that the treated infants spent significantly less time fussing and crying for the two minutes following the procedure but there was no effect on the cardiovascular response to pain. In a similar study undertaken in term infants, use of a

dummy produced a significant reduction in behavioural distress but there was no reduction in adrenocortical response (Gunnar et al. 1988).

In a quasi-random study, Campos (1989) compared the use of swaddling and dummies in two week old term infants undergoing heel prick blood sampling. The intervention period was for three minutes and infants were observed for a further three minute period post intervention. Both swaddling and dummies soothed the infants; heart rate and crying declined more rapidly in those who had a dummy but crying was more likely to resume when the dummy was removed than when swaddling ceased. Campos (1994) later compared the effect of rocking (held by the researcher and rocked in a rocking chair), dummy or routine care (no intervention) on the behavioural state of term infants undergoing heel prick blood sampling. Both dummies and rocking reduced crying with dummies predominantly producing sleep states and rocking quiet alert states.

It had been suggested that the use of dummies for preterm infants during painful procedures may create an association between non nutritive sucking and pain, which could interfere with the infant's future feeding ability (VandenBerg 1990; D'Apolito 1993).

The effect of swaddling on behavioural recovery in preterm infants was investigated by Frearon et al. (1997). They conducted a randomised crossover study of 15 preterm infants assigned to swaddling post heel prick blood sampling, routine care post heel prick blood sampling or no blood sampling and routine care. Infants less than 31 weeks gestation showed an immediate return to behavioural patterns similar to those during the no blood sample condition, regardless of treatment condition, possibly due to an inability to sustain negative behavioural states over a longer period because of immaturity. Infants 31 weeks or older showed prolonged behavioural disturbance after heel prick blood sampling, this was significantly reduced by swaddling.

Advances in knowledge regarding dummy use and pain or distress in infants have occurred. Sucrose has been investigated as a non-pharmacological intervention for relief of procedural pain in newborn infants and a Cochrane systematic review of 17 randomised controlled trials of this topic has been undertaken (Stevens et al. 2001). Various delivery methods were used to give the sucrose: syringe, dropper and dummy. Four of the randomised controlled trials included use of a dummy in the intervention. Carbajal et al. (1999) found that use of a dummy with or without sucrose was more effective than sucrose

alone (as administered by a syringe) in relieving behavioural distress associated with a painful procedure (venepuncture). However Gibbins et al. (2002) and Blass and Watt (1999) found that when sucrose was given with a dummy this was more effective than dummy alone. Whether sucrose alone provides a greater reduction in behavioural manifestation of distress or pain than a dummy (Blass and Watt 1999) or no difference in effect (in Stevens et al. 2001), is yet to be determined. Stevens et al. (1999) found a non significant trend towards a more beneficial effect of dummy use with sucrose than with dummy alone. Both these interventions were more beneficial than prone positioning or control.

2.9.2.4 Effect on breast feeding

In some developing countries dummies and bottles are not used at all for preterm infants as they are thought to interfere with establishing breast feeding (Narayanan 1990; Narayanan et al. 1991). The effect that the use of dummies may have on breast feeding success has not been evaluated in preterm infants.

2.10 Current interventions to support the transition to breast feeds

2.10.1 Feeding Tube only.

There have been two reports of using a 'no bottle' protocol with infants fed by gavage tube when the mother was not able to be present or when a top-up was required after a breast feed. The stated reason for implementing such a protocol was to avoid nipple or sucking confusion (Stine 1990; Gamble 1993). Stine (1990) conducted an audit of breast feeding prevalence over a 16 week period after implementation of a 'no bottle' protocol. Of 58 infants admitted during that time, 22 (38%) intended to breast feed and 36 (62%) to bottle feed; the number of mothers who commenced expressing is not stated. On discharge home 16 infants were partially and 11 exclusively breast feeding. The length of hospitalisation during a six week period, between those breast feeding (all using the no bottle protocol) and those fully bottle feeding, was identical, indicating that the absence of bottles did not delay the time taken to reach all sucking feeds. Neither of these authors has reported, however, whether a 'no bottle' policy made any difference to breast feeding prevalence (Stine 1990; Gamble 1993).

Using a no bottle protocol was found to be problematic for infants who were not satisfied with tube feeds and were unsettled after being deprived of a sucking/oral experience, (Jones 1994; Lang 1994). Jones' experience (1994) also suggests that infants' deprivation of regular suck-swallow experience led to a delay in establishing breast feeding.

During the time the research for this thesis was being conducted a randomised controlled trial was published, based on the no bottle protocol reported by Stine (1990). Bottle supplementation of breast feeds was compared with nasogastric tube supplementation in a randomised controlled trial involving 99 infants (Kliethermes et al. 1999). The study was undertaken in the United States of America in a private regional perinatal centre with a 40 bed Level III Intensive Care Unit. Eligibility criteria included the mother's decision to breast feed, birth weight between 1000 and 2500g, and age less than one week. Mother infant pairs were randomised to receive feeds by bottle or indwelling nasogastric tube for times when the mother was not available for a breast feed or if a supplement was required after a breast feed. Dummies were used for both arms. Outcome measures assessed were prevalence of breast feeding (partial and exclusive) at discharge from the intensive care nursery and at three days, three months and six months after discharge home.

Ninety-nine infants were enrolled in the study, 52 in the bottle group and 47 in the tube group. A sample size calculation was not reported. Random numbers were used to assign interventions, which were then mixed and drawn in random sequence after enrolment in the study. Allocation concealment was achieved by the use of sealed envelopes. It is not stated who implemented the randomisation. In the absence of clear reporting it is possible that selection bias could have occurred. It is not reported if those assessing the outcomes were blinded to group assignment. There is no indication of the number eligible for enrolment in the study, or the number who refused participation.

An intention to treat analysis was not undertaken. In total six were excluded from the bottle group and nine from the tube, leaving analysis on 46 in the bottle group and 38 in the tube group. The small number excluded from the analysis is unlikely to have affected the results significantly. The reasons for exclusion included non compliance (bottle group n=2; tube group n=3), neonatal complications, transfer to another institution and maternal complications.

There were differences in the baseline demographics between the groups, which were controlled for in the analysis. The tube group had more mothers who were older, had breast fed before and were wage earners; these are potential confounders for breast feeding success. The gestational age at birth of the infants was 26 to 35 weeks.

The results from this study showed that on discharge home from hospital, infants who were tube fed in the transition to breast feeds were 4.5 times more likely to be breast feeding (OR 4.5, 95% CI 1.4 to 15, P=0.0001). This included those who were partially and full breast feeding. The odds ratio of going home fully breast feeding in the tube group was 9.4 (95% CI 3.1 to 28.4). The positive effects persisted for all time periods (confidence intervals were not reported). At three days post discharge the odds ratio for any breast feeding was 5.0 and for fully breast feeding 6.4. At three months, those who were tube fed were 4.3 times more likely to have any breast feeding, and 3.8 times more likely to be fully breast feeding. The rate was not calculated for six months. To assess the length of breast feeding by group assigned, a multiple linear regression was done; on controlling for delivery type, the tube group breast fed an estimated average of 7.5 weeks longer than the bottle groups. This calculation does not take into consideration those who breast fed for longer than six months so should be interpreted with caution.

No adverse effects were reported for the longer period of nasogastric tube use. The tube group had the tube in situ for an average of seven days more than the bottle group. There was no difference in the duration of hospitalisation, or weight at discharge between the two groups.

The bottle group included eight pairs of twins and tube group had five pairs; one twin in each pair was selected at random and excluded in the analysis and the effect remained, although point estimates and confidence intervals were not reported. Cup feeding was used in this study only during the 'rooming-in' period prior to discharge when the nasogastric tube had been removed and a supplementary feed was necessary based on weight loss. No report was made of the number of times this was needed.

The intervention had a significant effect, however the confidence intervals are very wide. A larger sample size would be able to determine a more precise measure of effect for the intervention. The study was methodologically weakened by the small sample size, lack of intention to treat analysis and possibility of selection bias. The effect this would have on

the outcome, however, is likely to be small. Despite the methodological weaknesses, this study adds considerable weight to the hypothesis that bottle teats interfere with breast feeding success in preterm infants.

2.10.2 Cup feeding

Experience in the developing world, European and American neonatal units shows that cup feeding provides an alternative to bottle feeding for preterm infants who are unable to complete a breast feed or whose mothers are unable to be present for a breast feed (Armstrong 1987; Muhudhia and Musoke 1989; Musoke 1990; Jones 1994; Lang et al. 1994; BFHI News 1999; Gupta et al. 1999). Cup feeding is recommended as a feeding method for sick and low birth weight infants by the World Health Organisation and UNICEF (Lang et al. 1994). It has been suggested to be a useful alternative method in providing suck-swallow-breathing practice (Jones 1994; Lang et al. 1994). It was described and recommended as a method of feeding preterm infants as early as 1948 (Freeden 1948).

The technique for cup feeding a preterm baby has been described by Lang (Lang 1994) who introduced this method of feeding to the Exeter (UK) neonatal unit in 1989. Any cup can be used, most often a medicine cup. The baby is wrapped securely and supported in an upright sitting position. A cup, that is at least half full, is tipped so the milk is just touching the baby's lips; milk should not be poured into the baby's mouth. The rim of the cup is directed towards the upper lips and gums and the cup is left in this position during the feed. Preterm infants tend to 'lap' the milk when first commencing cup feeds, as they mature a sipping action develops (Lang 1994; Lang et al. 1994)

It is unknown why cup feeding may benefit breast feeding outcomes. For effective breast feeding the tongue needs to be extended over the bottom lip, this is essential for efficient stripping of the milk ducts (Woolridge 1986). Lang postulates that the tongue action required for cup feeding may promote the correct position of the tongue for breast feeding (Lang et al. 1994).

The potential benefits of cup feeding include: avoidance of any real or theoretical possibility of sucking confusion, the infant can pace their own intake of milk, and the use of lingual lipases for breakdown of dietary triglycerides (Lang et al. 1994). These reports

on cup feeding, while promoting avoidance of bottle teats, have not discussed the use of dummies in establishing breast feeds.

Clinical experience has found cup feeding to be safe, simple, practical and inexpensive (Armstrong 1987; Muhudhia and Musoke 1989; Musoke 1990; Jones 1994; Lang et al. 1994; Gupta et al. 1999). The physiological effects of breast and cup feeding were compared in a pilot study of 20 preterm infants born between 28 and 31 weeks gestation (Freer 1999). At the time the infants were studied they were between 31 and 35 weeks postmenstrual age, some infants were studied on more than one occasion. Sixty-four feeds were analysed (32 breast and 32 cup) on the following parameters: length of feed; burst length (run of sucks/laps with an interval of less than 1.5 seconds); pause length (interval > 1.5 seconds between sucks/laps); frequency of sucks/laps, swallows and breaths per feed; heart rate and oxygen saturation.

Congruent with earlier work comparing bottle and breast feeding (Meier and Anderson 1987; Meier 1988; Bier et al. 1993; Young 1995; Bier et al. 1997; Chen et al. 2000), Freer (1999) found differences in effect on the preterm infant between cup and breast feeding. Sucking during breast feeding was found to be more consistent and rhythmic than lapping/sipping during cup feeding. The breathing rate was decreased during sucking/lapping bursts in cup feeding with no difference in breathing rates during the pauses. There were longer pauses between sucking/lapping bursts associated with cup feeding, the authors suggesting the possibility of cup feeding requiring a greater respiratory recovery time. Swallow frequency was similar for both methods. There was a small, clinically non significant difference in oxygen saturation levels between the two feeding types, with breast feeding resulting in a slightly higher level (96%) than cup feeding (94%). With cup feeding there was a greater degree of variability in relation to the mean than with breast feeding indicating that a more stable oxygen saturation was maintained during breast feeding. There was a clinically insignificant difference in the mean heart rate between the two methods, 159 beats/minutes to 155 beats/minute. On further examination of individual feeding records the heart rate was found to be more stable during breast than cup feeding. The authors speculate that the feeding position may account for the differences in breathing rate, that is the upright position for cup feeding offers little chest support compared to the horizontal side-lying position for breast feeding.

Freer's (1999) work adds to the evidence that breast feeding is the most physiologically stable mode of oral feeding for preterm infants. The clinical significance of the physiological differences found between breast and cup feeding was minimal, except to highlight that infants need to be carefully observed during cup feeding and that breast feeding is the optimal method of sucking feed.

A comparison of the effects of cup and bottle feeding has been undertaken in preterm and term infants (Howard et al. 1999a; Malhotra et al. 1999; Marinelli et al. 2001). Marinelli et al. (2001) conducted a randomised crossover study of 56 infants less than or equal to 34 weeks gestation at birth, whose mothers intended to breast feed. The order of the first two non breast feeds, at post menstrual age greater than or equal to 34 weeks, was randomised to either one cup feed or one bottle feed, with a minimum of one gavage feed between. Average heart rate and respiratory rate increased in both methods, but was significantly higher during bottle feeding. Mean oxygen saturation was lower for bottle feeds (94.5%±5.3) than cup feeds (96.5%±2.6 P=0.02). Although statistically significant this difference is not clinically significant, however the lower margin of the range for bottle feeding was 74.4% compared to 90% during a cup feed which is of clinical importance. There was a significantly higher proportion of oxygen desaturations (less than 90%) during bottle feeds than during cup feeds is also of clinical importance

There were no differences in episodes of choking, spilling, apnoea or bradycardia between the two methods. Of interest was the high percentage of choking episodes with both methods (40% bottle feeds, 43% cup feeds). Volumes taken were significantly less with cup feeds (27.2 mls bottle, 20.9 mls cup, P=0.001) and it took longer to cup feed an infant than to bottle feed (20.1±5.9 minutes cup, 16.3±5.5 minutes bottle, P=0.002).

Similar results were found in a comparison of cup and bottle feeding in the term infant (Howard et al. 1999a). In this work the amount of milk ingested and the length of feeding time was compared between cup and bottle feeds and effects on infant stability were compared for infants' cup, bottle and breast feeding. Ninety-eight healthy term infants (day one to three) whose mothers did not wish to breast feed were randomised to receive either cup (n=51) or bottle feeds (n=47). Twenty five breast feeding term infants were used as a non randomised comparison. In contrast to preterm infants (Marinelli et al. 2001), the mean time taken to cup (5.3 ± 2.1 minutes) or bottle feed (5.9 ± 1.9 minutes) did not differ significantly. Breast feeding took longer (9.6 ± 3.5 minutes; P< 0.05) (Howard

et al. 1999a). The volume of feed ingested did not differ significantly between cup and bottle. Heart rate, respiratory rate and oxygen saturation also did not differ significantly between the two groups. When compared with the breast fed infants, cup and bottle fed infants had significantly increased overall heart rate ($P<0.001$), respiratory rate ($P=0.03$) and decreased oxygen saturation ($P=0.05$).

Malhotra et al. (1999) conducted a crossover study of the use of bottle, cup and paladai. The paladai is a traditional feeding device used in some South Indian communities. It is shaped like a small cup (30 ml capacity) with an open spout on one side to gently pour the milk into the infant's mouth. 100 infants were enrolled in the study (66 term, 20 growth retarded and 14 preterm). All three methods were tried on each baby; outcomes assessed were volume taken, duration of feed and degree of spilling. In contrast to Marinelli's (2001) findings, the preterm infants ingested the most milk with the paladai, then cup and the least by bottle. They also took the least time to feed with the paladai, then cup and the slowest feeds were by bottle. Spilling was greatest with the cup and least with the bottle.

Dowling et al. (2002) published a case-series of eighteen cup feeding sessions in eight preterm infants (mean gestational age at birth 30.6 weeks). Oxygen saturation remained 90% or greater during cup feeding. The mean duration of feeds was 15.6 minutes (SD 3.9) but the volume of intake was low (mean 4.6 mls, SD 2.2ml, range 1.5 to 8). In two thirds of the feeding sessions the infants spilled milk on to the bib, which amounted to 39% of the volume that had been removed from the cup. The authors conclude that although infants remain physiologically stable cup feeding is of *'questionable efficacy and efficiency'* (p 13) due to the considerable amount of spillage (Dowling et al. 2002).

The above studies confirm reports of clinical experience that cup feeding is as safe, if not safer, than bottle feeding in preterm and term infants.

Data from the Exeter neonatal unit (Lang et al. 1994) showing historical comparisons between preterm infants who have been supplemented with cup feeds and those who had bottles, suggest a significant increase in the prevalence of exclusive breast feeding for the cup fed babies on discharge home (81% compared with 63%). The only known major difference between the two groups was in the method of feeding, which suggests that cup feeding can contribute to the establishment of successful breast feeding. However there may well be unknown differences between these comparative groups who self selected

their method of infant feeding, or changes in staff practices, that could account for the differences observed.

Five randomised controlled trials of cup feeding were published during the period of this research, two with preterm infants (Mosley et al. 2001; Rocha et al. 2002), and three in term infants (Schubiger et al. 1997; Kramer et al. 2001b; Howard et al. 2003). Mosley et al. (2001) conducted a small pilot study of bottle compared with cup for supplementary feeding of preterm infants (32 to 37 weeks gestation) whose mothers intended to breast feed. Sixteen infants were recruited and fourteen analysed; eight received supplementary feeds by bottle and six by cup. Six out of the eight bottle fed infants were exclusively breast fed on discharge compared with four of the six cup fed infants. This sample size is too small to draw any conclusions on the effect supplementary cup or bottle feeds may have on breast feeding outcomes, the authors however have shown that a randomised controlled trial is feasible (Mosley et al. 2001).

Rocha et al. (2002) conducted a randomised controlled trial in the preterm infant population with the objective of examining the impact cup feeding has on subsequent breast feeding. The study was conducted in a Brazilian Neonatal Intensive Care Unit. Eligibility criteria included clinically stable singleton infants, not requiring intensive care or parenteral nutrition and born between 32 and 36 weeks gestation with weight less than 1700 grams and mother intending to breast feed. The outcomes assessed were breast feeding prevalence on discharge home and at three month follow-up, weight gain and oxygen saturation during feeding. A power calculation was not reported. Infants were fed via an orogastric tube until reaching 1600 grams; breast feeding was then encouraged. Infants were cup fed (experimental group) or bottle fed (control group) when breast feeding could not occur or when supplementation was required after a breast feed. Infants in the cup feeding group were not offered a dummy; non nutritive sucking was provided by offering the little finger.

The infants were stratified according to weight categories: 500g to 999g, 1000g to 1499g and 1500g to 1699g. Randomisation occurred by the drawing of lots. It is not stated who recruited participants or who assigned the participants to the groups. It is not reported if the outcome assessors were blinded to treatment assignment. The number eligible, number refused and number ineligible were not reported. Thirty seven infants were randomised to the bottle feeding group and 46 to the cup feeding group. An intention to treat analysis

was not performed. Three infants were excluded from analysis in the bottle feeding group, two because of the infants' medical condition (gastro oesophageal reflux, severe bronchopulmonary dysplasia) and a third infant whose mother was using cocaine. Two infants were excluded from the cup group, one for non compliance and one due to complications of bronchopulmonary dysplasia. Analysis was done on 34 in the bottle group and 44 in the cup group.

Infants exclusively or partially breast fed directly at the breast were defined as breast feeding. There were small absolute differences in the proportion of infants breast feeding on discharge home (bottle n=27, 79%, cup n=36, 82%). at the first outpatient visit at 5 to 15 days post discharge (bottle n=15, 56%, cup n=19, 57%) and at three months post discharge (bottle n=5, 15%, cup n=13, 30%). Confidence intervals were not reported. The study was underpowered; a sample size of 48 in each arm would have been able to detect a 21% increase in breast feeding from 79% to 100% at discharge home. 134 in each arm was needed to confidently determine if the difference found at three months post discharge was significant.

Schubiger et al. (1997) conducted a randomised controlled trial in the term infant population with the objective of examining the need for adherence to steps six and nine of the UNICEF/WHO 'Baby Friendly Hospital Initiative' (BFHI). The BFHI consists of 10 steps aimed at providing the best environment for supporting women choosing to breast feed (WHO/UNICEF 1989). Step six states: 'Give newborn infants no food or drink other than breast milk' and Step 9: 'Give no artificial teats or pacifiers to breast feeding infants'. Although the results of this study cannot be generalised to preterm infants' transition to breast feeds, it is important to consider, as it was the first randomised controlled trial to study the use of artificial teats in breast feeding.

This multicentred trial involving 602 infants was conducted in ten Swiss maternity units where it is accepted practice to offer newborn infants fluid supplements (10% Dextrose) by bottle after breast feeding and offer dummies to all infants without restriction. Eligibility criteria included gestation greater than 37 weeks, birth weight 2750g to 4200g, mothers' intention to stay in the hospital for five days and the mothers planned to breast feed for greater than or equal to three months. The hospitals that participated also had an established breast feeding program including early initiation of breast feeding, lactation consultants, rooming-in and restricted use of formula supplements. The study had 95%

power to detect a 10% difference in breast feeding outcomes at two months of age based on a two month breast feeding rate of 90%. The outcomes assessed were breast feeding prevalence at five days, two months, four months and six months.

The intervention assessed was termed the UNICEF group. Supplements were given by cup or spoon if medically indicated (infants agitated or screaming after breast feeding, blood sugar level <2mmol/l, no urine output over a four hour period). Bottles, teats and dummies were not allowed. The control group continued their standard practice, supplements were offered by bottle after breast feeds and dummies were offered to all infants. In both groups, the supplement offered during the first few days was a 10% dextrin-maltose solution. Infant formula was only used from day four to five if the infant had lost greater than 8% of their birth weight and if there was evidence of insufficient lactogenesis.
No details of the randomisation process are reported, that is, sequence generation, allocation concealment or implementation. It is not reported if the outcome assessors were blinded to treatment assignment. The number eligible, number refused and number ineligible are also not reported. 294 infants were randomised to the UNICEF group and 308 to standard care.

Of particular interest in this study was the high rate of non compliance. In the UNICEF group 114 (39%) did not comply with the treatment protocol: 28 (9.5%) requested to use a bottle or found cup or spoon feeding too difficult, and 70 (24%) wanted to use a dummy. Analysis was not done on intention to treat; those who did not comply were excluded leaving 180 from the UNICEF group and 291 from the standard group. No significant differences in breast feeding outcomes at any of the time periods were reported: (UNICEF versus standard) day 5: 100% versus 99%; two months 88% versus 88%; four months: 75% versus 71%; six months 57% versus 55%. When the 70 infants in the UNICEF group who had a dummy were included in the analysis, the breast feeding prevalence showed little difference: two months, 87.7%; four months, 74%; six months: 58.9%.

This study does not support the theory of *nipple confusion* in term infants with both intervention and treatment groups having a very high prevalence of breast feeding. It also highlights difficulties that can be encountered when trialing a new therapy in an area with entrenched beliefs and practices. The authors postulated that a possible contributor to the high drop out rate was that women in the same room or ward had been randomised to differing methods.

A further randomised controlled trial has been conducted with term infants with the experimental intervention modelled on the BFHI (Kramer et al. 2001b). The objective of this study was to assess the effects of breast feeding promotion on breast feeding duration and exclusivity and gastrointestinal and respiratory infection and atopic eczema among infants. This cluster randomised controlled trial conducted in the Republic of Belarus. Staff in the hospitals randomised to the experimental intervention received training in BFHI lactation management and policies and procedures were changed to be consistent with the BFHI. This would include adherence to Step Nine: 'Give no artificial teats or pacifiers to breast feeding infants'.

Thirty-two hospitals participated, 16 randomised to the experimental intervention and 15 to standard care. The number of mother-infant pairs enrolled was 17,046 with 16,491 (96.7%) completing the 12 month follow-up. Eligibility criteria included the mother's stated intention to breast feed, and a term healthy singleton infant. Breast feeding duration was assessed at three, six, nine and twelve months of age. WHO definitions of breast feeding were used.

They estimated that the BFHI intervention would reduce breast feeding discontinuation by three months from 50% to 35%. A sample size of 500 mothers and infants enrolled at each hospital, and using 15 pairs of study sites (15,000 mother-infant pairs) would provide greater than 80% power to detect such a difference at a two sided alpha level of 0.05.

An intention to treat analysis was used for all outcomes. Infants from the intervention sites were more likely than control infants to be breast fed to any degree at three months (72.7% versus 60%; adjusted OR for having been weaned 0.52; 95% CI 0.40 to 0.69), at six months (49.8% versus 36.2%; OR for having been weaned 0.52; 95% CI 0.39 to 0.71), at nine months (36.1% versus 24.4%; OR for having been weaned 0.51; 95% CI 0.36 to 0.73), and at 12 months of age (19.7% versus 11.4%; OR for having been weaned 0.47; 95% CI 0.32 to 0.69). The intervention group were significantly more likely to be exclusively breast fed at three months (43.3% versus 6.4%; P<0.001) and at six months (7.9% versus 0.6%; P=0.01) (Kramer et al. 2001b).
The intervention, modelled on the BFHI, significantly increased the duration and exclusivity of breast feeding in the first year of life. The authors have not stated whether the use of artificial teats was standard practice and as such whether it formed part of the standard care for the control group. They have stated that the hospital practices in Belarus

resembled practices of North America and Western Europe 20 to 30 years ago (Kramer et al. 2000; Kramer et al. 2001b). Use of formula feeds and dummies were promoted at that time. If the use of artificial teats was part of standard care, the extent this changed with the intervention is not reported. Although the 'package' of the BFHI ten steps increased breast feeding prevalence; the effect of the individual components has not been assessed.

Howard et al's (2003) study has been described in section 2.9.1. A randomised controlled trial was conducted to evaluate the effects of dummy use and in-hospital cup feeding and bottle feeding on breast feeding in term infants. Seven hundred women were randomised to one of four interventions: bottle/early dummy, bottle/late dummy, cup/early dummy, cup/late dummy. Supplemental feeds were only given if needed and according to randomised allocation, cup or bottle.

Supplementing breast feeds in hospital reduced breast feeding duration, however it did not make any difference whether the supplemental feeds were given by cup or bottle. In an analysis by number of supplementary feeds, when three or less were given there was no significant effect on breast feeding duration, when greater than three were given, cup feeding significantly improved exclusive and full breast feeding duration but not any breast feeding. Infants of women who delivered by caesarean section, who were given supplemental feeds by cup were breast fed for a median of 10 weeks longer than similar women whose infants had supplemental feeds given by bottle. These infants received more supplemental feeds than infants born vaginally.

The authors conclude that in term infants it is important to avoid supplementing breast feeds unless medically indicated. If supplements are necessary the authors recommend that these should be given by cup (Howard et al. 2003).

2.11 Breast feeding definitions

Breast feeding definitions for healthy term infants were developed by the Interagency Group for Action on Breastfeeding in 1988 and published by Labbok and Krasovec (1990). Standardised breast feeding definitions were needed to enable meaningful comparisons of breast feeding patterns on infant nutrition, health and maternal fertility.

Their definitions categorise breast feeding into full, partial and token.

Full breast feeding includes:

- exclusive breast feeding (no other liquid or solid is given), or
- almost exclusive (vitamins, minerals, water, juice or ritualistic feeds are given infrequently in addition to breast feeds).

Partial breast feeding is categorised into:

- high (greater than 80% of feeds are breast feeds),
- medium (20-80% are breast feeds), and
- low (less than 20% are breast feeds).

Token breast feeding includes minimal, occasional or irregular breast feeds.

The Labbok and Krasovec (1990) schema has since been modified to include further sub categories (Coffin et al. 1997). Full, Partial and Token Breast feeding have been maintained and an alternate categorisation of 'Full/Nearly Full breast feeding' and 'Low Partial/Token breast feeding' has been added giving an alternate three categories of:

- Full/Nearly Full breast feeding (includes Exclusive, Almost exclusive and High Partial breast feeding)
- Medium Partial breast feeding
- Low Partial/Token breast feeding (includes Low partial and token breast feeding).

Breast feeding has not been specifically defined within the schema (Labbok and Krasovec 1990; Coffin et al. 1997), that is, does breast feeding include provision of expressed breast milk or is it feeding directly from the breast only? Labbok and Krasovec (1990) do suggest that in addition to their breast feeding schema, a more complete description of breast feeding behaviours is recorded. They present a list which includes the following points:

> - artificial nipples and other devices, which would include information on the use of any other nipple, pacifier or other feeding devices (spoons, cup and so forth);
>
> - expression of breast milk and later use, or the percentage of feeds given as expressed milk. (p. 228).

This implies that breast feeding includes the consumption of human milk by other feeding devices.

There is some contention over the definition of breast feeding. In an editorial discussing Labbok and Krasovec's (1990) breast feeding definitions, Armstrong (1991) argues that the alternate phrase *'fed exclusively on breast milk'* (p52) should not be incorporated into exclusive breast feeding as this will introduce a level of complexity when analysing the effects of *'the intimate physiological and psychological bonding of breast feeding'* on infant development and maternal fertility as it would allow for the use of bottles, donor milk or wet nursing.

The World Health Organisation (1991) developed definitions of key breast feeding indicators with categories are based on those published by Labbok and Krasovec (1990). However, the World Health Organisation's definition of breast feeding includes the provision of expressed breast milk, namely: *'the child has received breast milk (direct from the breast or expressed)'* (1991 p. 2). They distinguish between feeding directly from the breast and expressed breast milk from bottles by including a definition of bottle feeding: *'any liquid or semi-solid food from a bottle with nipple/teat. Also allows breast milk by bottle'* (World Health Organisation 1991 p 3)

In two studies of breast feeding patterns and problems of low birth weight infants the following definitions of Labbok and Krasovec (1990) were used (Hill et al. 1994; Hill et al. 1997).

- Exclusive human milk feeding (at breast or expressed breast milk by bottle)
- High partial human milk feeding (greater than 80% human milk)
- Medium partial human milk feeding (80-20% human milk)
- Low partial human milk feeding (less than 20% human milk)
- Token (minimal, occasional breast milk feeding)

The majority of hospitalised preterm infants receive oral vitamin and mineral supplements, I would suggest that Hill's (1994; 1997) use of the term 'exclusive human milk' feeding equates to Labbok and Krasovec's (1990) term 'full breast feeding' which allows for the inclusion of vitamins, minerals etc.

Labbok and Krasovec's (1990) breast feeding categories were used for the research reported in this thesis and information was collected on mothers who chose to express and bottle feed their infant/s. Breast feeding was defined as the provision of mother's milk by direct breast feeding or other feeding device (World Health Organisation 1991; Hill et al.

1994). Since then there has been further discussion in the literature about the suitability of these definitions for the preterm population. In a letter to the editor, Meier et al. (1997) express concern that the definitions do not accurately describe the breast feeding situation for preterm infants. They argue that mothers of preterm infants frequently provide expressed milk for all of their infant's feeds but not from direct breast feeding. They would be classified as fully breast feeding using the Labbok and Krasovec schema, but the mothers may not have met their goal of directly breast feeding their baby. Meier and colleagues are undertaking a research project to accurately describe the breast feeding practices for preterm infants.

Kliethermes et al. (1999) in their randomised controlled trial of nasogastric tube supplementation compared with bottle supplementation in the transition to breast feeds for preterm infants used Labbok and Krasovec's (1990) breast feeding definitions. However, if an infant in either group received complementary or supplementary human milk they were considered as partially breast fed.

In view of the evidence available at the time this study was designed, Labbok and Krasovec's (1990) breast feeding categories were used and breast feeding was defined as the provision of mother's milk by direct breast feeding or other feeding device (World Health Organisation 1991; Hill et al. 1994).

2.12 Conclusion of the literature review

When this research was conceptualised and implemented there were no randomised controlled trials of the use of artificial teats (dummies or bottle) in either the preterm or term infant population. There was strong evidence from observational data to suggest dummy use was associated with a reduction in breast feeding duration in term infants. The safety of cup feeding was based on reports of clinical experience. Since then, cup feeding has been shown to be safe in the preterm population (Marinelli et al. 2001). Randomised controlled trials have shown conflicting outcomes for the effect dummy use has on breast feeding in term infants (Kramer et al. 2001a; Howard et al. 2003). Rocha et al. (2002) showed no difference in breast feeding outcomes in preterm infants when comparing cups and bottles. Schubiger et al. (1997) and Howard et al. (2003) also showed no difference in breast feeding outcomes with use of bottles in term infants. There have been no randomised controlled trials of the use of dummies in the preterm population and no large

studies of the use of cups. The randomised controlled trial and systematic review reported here, therefore, are potentially important and timely.

Chapter 3. Methods: Randomised controlled trial

3.1 Study design

The study design was a parallel randomised 2 x 2 factorial trial.

3.1.1 Study design rationale

A randomised controlled trial is the optimal research method available to evaluate questions of treatment effectiveness (Elwood 1998; Clarke et al. 2003). The random allocation of participants means that every participant has the same chance of being allocated to the control or treatment group, it also increases the likelihood of achieving similar distribution of known and unknown baseline characteristics (Jadad 1998).

3.2 Participants

3.2.1 Eligibility Criteria

Infants admitted to Neonatal Intensive (Level III) or Special Care (Level II) nurseries were eligible for inclusion in the study if they met the following criteria:

- gestational age at birth less than 34 weeks
- had not been fed by bottle or cup
- had not used a dummy, or if a dummy had been introduced it had been available to the baby for less than or equal to 48 hours
- the mother stated a desire to breast feed

Twins were eligible for inclusion.

Excluded were infants with major congenital abnormalities that precluded enteral feeding, and triplets or higher order births.

3.2.1.1 Eligibility Criteria rationale

The study was limited to infants less than 34 weeks gestation at birth as they have a longer hospital stay and therefore more exposure to supplementary and complementary feeding.

Infants greater than or equal to 34 weeks gestation at birth are more mature with a developed suck swallow breath reflex and shorter hospital stay.

At the commencement of the study, an infant who had any dummy use was excluded. However, especially in the initial stages of the study, staff would automatically put a dummy in the cot, as this was standard practice. Whether the baby had used the dummy or not was difficult to determine accurately. It was decided that excluding infants who had a dummy available for less than or equal to 48 hours would make recruitment difficult and the amount a baby used a dummy in the first one to two days was judged to be minimal.

3.2.2 Settings and location of study

Recruitment took place at the Women's and Children's Hospital (WCH), Adelaide, South Australia and the Mercy Hospital for Women (MHW), Melbourne, Victoria. The WCH has 14 ventilator tertiary care cots, and 35 Special Care (non-ventilated) cots. The tertiary level nursery deals with approximately 60% to 70% of South Australia's infants needing that level of care. The WCH nurseries had 1,107 admissions in the year 2000; this includes term and preterm infants (279 to Neonatal Intensive Care and 828 to Special Care).

The MHW has a large tertiary level nursery with 10 ventilator cots, 13 High Dependency and 30 Special Care. The MHW had 1,073 admissions in the year 2000.

Approximately two thirds of infants admitted to the WCH and MHW are transferred to peripheral Level II and Level I hospitals for follow-on care. 54 peripheral hospitals participated in the research (Appendix I: Participating peripheral hospitals).

The study was planned to be undertaken only at the WCH, but due to a slower than anticipated recruiting rate a second study site was sought at the MHW.

3.3 Interventions

Consenting mothers and their infant/s were randomised to one of four groups:

- Cup and No dummy,
- Cup and Dummy,
- Bottle and No dummy

- Bottle and Dummy (standard care)

The group to which the mother/infant pair was allocated was recorded on the problem sheet of the infant's case notes and on the nursing care plan. An identifying label was placed on the cot or incubator.

The intervention was for the duration of hospital stay only, including at peripheral hospital.

3.3.1 No dummy groups

Alternate soothing methods promoted for those randomised to No Dummy included:

- facilitation of hand to mouth action for the infant, promoting self quieting behaviour
- containing, swaddling, rocking, or holding the infant
- use of baby slings
- non nutritive sucking to the breast when the mother can be present
- feeding schedules that allow the infant to be fed earlier than the prescribed feeding time if the infant is demanding.

3.3.2 Cup feeds

Infants in the cup feeding groups were fed by cup according to the hospital cup feeding standard (Appendix II: Cup feeding standard). This standard is based on the work of Lang (1994). The cup used was a medicine cup (60 ml capacity) otherwise known in the nurseries as a gavage cup. Staff and parents were taught how to cup feed according to the cup feeding standard.

Cup feeding commenced when the infant was assessed to be mature enough to coordinate a suck/swallow/breathe reflex, at the same point as bottle feeding would have been introduced. Lang (Lang 1994; Lang et al. 1994) has reported that infants can cup feed at a much earlier gestational age than bottle feeds, however this did not form part of this research.

Feeding by cup occurred whenever the mother was unable to be present for a breast feed or additional milk was required after a breast feed and the attending midwife or nurse assessed that this should be given orally.

3.3.3 Standard care – dummy and bottle

A dummy was made available to infants on admission to the unit. Dummy use was encouraged during gavage tube feeds and when the infant was restless or distressed.

Bottle feeding commenced when the infant was assessed to be mature enough to coordinate a suck/swallow/breathe reflex. Infants were fed by bottle as per current standard care within the nurseries.

Feeding by bottle occurred whenever the mother was unable to be present for a breast feed or additional milk was required after a breast feed and the attending midwife or nurse assessed that this should be given orally.

3.3.4 Treatment schedules

The following was standard care for all infants:

- informing all mothers of preterm infants of the benefits to their infant of breast milk.
- supporting the mother in expression of breast milk with one to one education plus written information.
- providing information to the mother on maintenance of her milk supply including frequency of expressing, expressing technique and the use of Maxolon.
- encouraging parental involvement with and participation in the care of their baby. This includes changing nappies, doing daily washes etc.
- promoting skin-to-skin contact, including nutritive and non nutritive sucking to the breast.
- providing letters and photographs to mothers who could not be with their infant for periods of time.

Neither the bottle nor cup was to replace a breast feed unless the mother was unable to be present and the first sucking feed in both groups should be a breast feed. In both groups if the prescribed volume was not taken by cup/bottle this was then given via indwelling nasogastric tube.

3.4 Ethical considerations

A randomised controlled trial was required as there was inconclusive evidence of the true effects of non nutritive sucking of a dummy and of cup feeding on establishing breast feeds in preterm infants. Ethical approval was granted for the study by the research and ethics committees of the WCH, MHW, University of Adelaide and the participating Victorian hospitals.

Ethics approval was not sought from participating peripheral hospitals in South Australia; the midwifery and medical heads granted permission to continue the study in their hospitals given that ethics approval had been granted by the WCH and infants had been transferred from this institution.

Women and their infant/s were entered into the trial if signed, informed consent was given (Appendix III: Consent form). See section 3.9.3 for details of recruiting process.

3.5 Preparation and ongoing support

3.5.1 Staff education

Cup feeding had not been practiced at the WCH. In-service sessions were conducted and one-to-one support was provided where needed, before commencing the trial and continued during the trial. Written instructions and supporting literature were readily available. Ongoing support was available from the researcher.

Cup feeding had been practiced at the MHW for approximately three years before its participation in the trial. The research assistant at the MHW was a lactation consultant and provided in-service education plus one on one support to the staff.

Written instructions and supporting literature were available to all participating peripheral hospitals. An in-service education session and telephone support were given to the city hospitals participating in the Adelaide area. Support for South Australian country hospitals was by telephone only. Support for participating Victorian peripheral hospitals was by telephone and written information only.

Updates were provided through the ward communication book at the WCH and a newsletter to both participating centres.

3.6 Outcomes

3.6.1 Primary outcomes

- Proportion of infants fully breast feeding on discharge home
- Proportion of infants with any breast feeding (fully and partially) on discharge home

3.6.2 Secondary outcomes

- Proportion of infants breast feeding at three and six months post discharge.
- Number of days to all sucking feeds
- Duration of hospitalisation
- Weight gain
- Feelings about participation in the trial

3.7 Data collection

3.7.1 Baseline demographic and clinical characteristics

A questionnaire was given to mothers on entry to the trial to determine baseline demographic information (Appendix IV: Maternal questionnaire). Maternal and neonatal data were also collected from case notes to determine baseline demographic and clinical characteristics of the participants. The following information was sought: sex, birth weight, diagnosis, number of ventilator days, number of nasal continuous positive airway pressure (CPAP) days (Appendix V: Discharge data sheet (discharge home/transfer from recruiting hospital). Data were also collected on use of lactogogues (Maxolon), nipple shields, and supply lines.

Clinical definitions used were based on those of the Australian and New Zealand Neonatal Network (Australian & New Zealand Neonatal Network 1996).

3.7.2 Primary outcomes

Labbok and Krasovec (1990) breast feeding definitions were used for the primary outcomes:

- Full breast feeding (vitamins, minerals, water, juice or ritualistic feeds are given infrequently in addition to breast feeds)
- Partial breast feeding: High partial (greater than 80% of feeds are breast feeds)
  Medium partial (20-80% are breast feeds)
  Low partial (less than 20% are breast feeds)
- Token breast feeding (minimal, occasional breast feeds).

The prevalence of partial breast feeding was estimated from the fluid balance chart as follows:

- High partial – nine of the last ten feeds were breast feeds
- Medium partial – two to eight of the last ten feeds were breast feeds
- Low partial – nine of the last ten feeds were formula

In this study breast feeding was defined as the provision of mother's milk by direct breast feeding or other feeding device (World Health Organisation 1991; Hill et al. 1994). This definition of breast feeding therefore included women who chose to express and bottle or cup feed.

For comparison purposes the three partial feeding and token categories were collapsed into one category called 'partial breast feeding', leaving three comparative groups:

1) Full breast feeding
2) Partial breast feeding
3) Not breast feeding

Note was taken of women who chose to express and bottle feed their infant/s. For infants discharged home from the WCH or MHW, data were collected from the case notes on discharge from the hospital. For infants who were discharged home from peripheral hospitals, data were obtained either via telephone to the hospital staff, completion of a form by peripheral hospital staff or the researcher accessing case notes.

3.7.3 Secondary outcomes

The time period three and six months post discharge was selected rather than three and six months of chronological age as nutritional and developmental assessments of preterm infants are recalculated to corrected age, the age they would be if born at term. Some of the very preterm infants may not have been discharged home from hospital at three months of age, for example an infant born at 24 weeks gestation and discharged home at the term equivalent post menstrual age of 38 weeks would be 3½ months of age.

A questionnaire was sent to mothers at three and six months post discharge to assess their breast feeding status and feelings about participating in the trial. The three month questionnaires for each study group were similar differing only for specific questions relating to particular study allocation (question 16) (Appendix VI: Three month questionnaire (form 2A, 2B, 2C, 2D)). The six month questionnaire differed depending on breast feeding status at three months. If a woman was not breast feeding at three months a shortened questionnaire was used (Appendix VII: Six month questionnaire (form 3A, 3B)). Women were asked to indicate the type of milk or combination of milk their infant/s received in the previous 24 hours: breast milk only, breast milk and formula or formula only. If they were receiving breast milk and formula they were asked to indicate the proportion of each as follows: more than half milk feeds are breast milk the rest are formula; about half milk feeds are breast milk and half formula; less than half milk feeds are breast milk, the rest are formula.

Data were collected from case notes to calculate the total duration of hospitalisation. This included the number of days at WCH/MHW plus the peripheral hospital. The number of days to reach full oral feeds was calculated as days from birth to final gavage tube feed. Weight gain was calculated in grams per kilogram per day as follows:

Grams per kilogram per day = grams per day/average weight

where *Grams per day = (discharge weight – birth weight)/length of stay*

and *Average weight = (birth weight + discharge weight)/2*

For those not breast feeding at the time of the three month and six month questionnaire reasons for stopping were sought. These consisted of structured items, with an 'other' open ended category. These were based on reports in the literature of reasons for stopping breast feeding in preterm and term infants (Hill et al. 1994; Stamp and Crowther 1995) and from clinical experience.

3.7.4 Questionnaire administration and follow up

The questionnaires were pilot-tested on the first ten women in the study and required some minor grammatical changes.

The demographic questionnaire was given to mothers on entry to the trial, generally while still an in-patient. The three and six month post discharge questionnaires were mailed to the participants with an enclosed reply paid envelope. A follow up telephone call was made if the questionnaire was not returned; the questionnaire was then either completed over the telephone, or another questionnaire sent.

3.8 Sample size

The sample size was calculated on the expected number of infants less than 34 weeks gestation that could be recruited over a two year period from the WCH. Allowing for a 20% non recruitment rate, and including infants transferred to peripheral hospitals, this number was 310. With $P<0.05$ and 80% power a sample size of 310 would detect a 16.5% increase in the rate of those fully breast feeding compared to partially and not breast feeding at discharge, (from 45% to 61.5%) between dummy use and no dummy use (irrespective of cup or bottle use) and between cup and bottle (irrespective of dummy use). The sample size available for the combined effect of cup ± dummy and bottle ± dummy limits the ability of this study to detect smaller, clinically significant rates of change in breast feeding.

The baseline fully breast feeding rate of 45% was based on the number of infants discharged home fully breast feeding from the WCH averaged over the preceding five years prior to the commencement of the study.

3.9 Randomisation

3.9.1 Sequence generation

The randomisation schedule was developed using a random number table to select balanced blocks of varying size with stratification for gestation less than 28 weeks and 28 to less than 34 weeks. The mother was the unit of randomisation. A separate randomisation schedule was developed for the WCH and MHW.

3.9.2 Allocation concealment

The assignments were enclosed in sequentially numbered, opaque, sealed envelopes and administered away from the wards involved in the study.

3.9.3 Implementation

An independent researcher developed the randomisation schedule and secured the assignments in opaque envelopes.

Eligible women were invited to participate in the study by the researcher at the WCH or research assistant at the MHW. Women were approached as soon as possible after the birth of their baby depending on the clinical status of their baby. Attending nurses or midwives were consulted as to the appropriate timing of the approach. A study information sheet was given to potential participants and they were counselled about the study (Appendix VIII: Parent information sheet). At times the attending midwife or nurse approached and enrolled eligible participants. Women were entered into the trial if signed, informed consent was given.

Twenty four hour treatment allocation was available by telephoning an independent ward within the hospital (Rose ward at the WCH and Ward Nine at the MHW). On confirming eligibility and gestation, the next sequential envelope was opened and treatment group assigned (Appendix IX: Trial entry form).

As the mother was the unit of randomisation twins were assigned to the same group.

3.10 Blinding

The nature of the study meant that the participants, care providers and the researcher were unable to be blinded to treatment allocation. The researcher undertook data entry and analysis.

3.11 Analysis and Statistical methods

Data were entered into Microsoft Access 97 by the study investigator. Data were analysed using Stata (Release 7) (StataCorp 2001) and undertaken by the study investigator.

All analyses were performed on an intention to treat basis. Initial analysis examined the baseline characteristics of the randomised infants. Outcome analysis primarily used logistic models to estimate odds ratios and 95% confidence intervals. The dependence due to inclusion of twins was accounted for by using robust variance estimates.

Adjustment to the model was specified a priori and was made where there was a greater than or equal to 10% difference in the distribution of a variable between the groups and for known confounding. Previous research has indicated that maternal education, prior breast feeding experience and gestational age influence breast feeding performance and duration (Kaufman and Hall 1989; Yip et al. 1996; Boo and Goh 1999; Nyqvist and Ewald 1999; Killersreiter et al. 2001; Furman et al. 2002).

3.11.1 Primary outcomes

The two principal hypotheses were tested using a logistic model with indicator variables for Cup/Bottle and Dummy/No Dummy, and also an interaction term. The interaction was not significant or important to the model permitting a reduced model to be used. This reduced model is used to test for the marginal differences between Cup and Bottle and between Dummy and No Dummy use on the primary outcomes. Each of the hypotheses was tested at the 0.05 level.

3.11.2 Secondary outcomes

The proportion of infants breast feeding at three and six months post discharge was tested using a logistic model as explained for the primary outcomes. Survival analysis was used to assess the difference between the groups in the number of days to reach all sucking feeds and duration of hospitalisation. The effect was expressed as a relative hazard and 95 per cent confidence interval; the estimate of the relative hazard was derived by Cox proportional-hazards regression. The dependence due to inclusion of twins was accounted for by using robust variance estimates. Adjustment to the model was specified a priori and was made where there was a greater than or equal to 10% difference in the distribution of a variable between the groups and for gestational age at birth which directly influences the time taken to reach all sucking feeds and length of hospital stay.

3.11.3 Primary and secondary outcomes by recruiting hospital

Exploration of the primary and secondary outcomes were undertaken by recruiting hospital to explore possible heterogeneity across recruiting sites. The primary outcomes were tested using a logistic model with indicator variables for recruiting hospital and Cup/Bottle or Dummy/No Dummy and also an interaction term. The a priori hypotheses did not entail a recruiting centre specific effect and the study is underpowered to detect such an effect. The main results, therefore, are based on the overall data.

Chapter 4. Participant flow and baseline data

4.1 Recruitment period

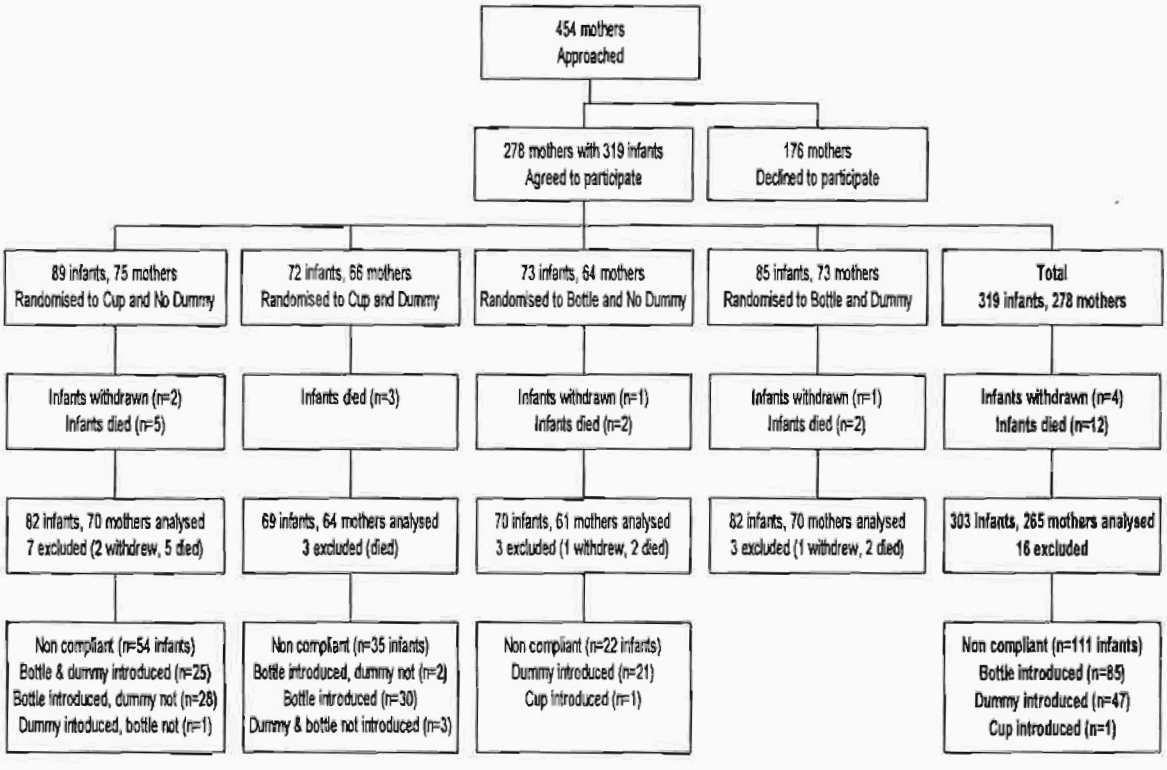
Recruiting took place at the WCH from April 1996 to December 1998. The recruitment rate at the WCH was not as high as anticipated with approximately 50% of those eligible not willing to participate. Other collaborators were sought; participants from the MHW were recruited from May 1998 to November 1999.

4.2 Participant flow

4.2.1 Numbers randomly assigned

Four hundred and fifty four women were approached to participate in the study, 278 mothers with 319 infants agreed to participate and were randomised as shown in Figure 4.1. One hundred and eight infants were recruited from the WCH and 211 from the MHW.

Figure 4.1 Participant flow



In Table 4.1 the reasons for not participating in the study are outlined. The main reason given was that the mother wanted her baby to have a dummy (n=45, 27%). In contrast

14% (n=23) chose not to participate because they did not want their baby to have a dummy. For 22% (n=36) of the mothers, the study did not appeal to them. Six mothers felt their baby had already been through enough and did not want to have anything extra done to them. For 17 (10%) mothers the process of randomisation did not appeal, with 12 of these mothers wanting their baby to be able to have whatever they needed and would help them without being restricted by a study protocol. Five mothers wanted to be able to choose the group to which their baby would be allocated.

Table 4.1 Reasons for not participating in the study

Reasons for non participation (n=164)*	**No (%)**
Dummy:	
Staff advised to have a dummy	2 (1)
Did not want baby to have dummy	23 (14)
Wanted baby to have a dummy	45 (27)
Bottle:	
Wants baby to have a bottle (promote sucking)	16 (10)
Does not want baby to have a bottle	9 (6)
Wants to express & bottle feed	2 (1)
Disagrees with cup	7 (4)
Other:	
Will only be expressing while baby sick	6 (4)
Time - "too much going on"	3 (2)
Doesn't appeal	36 (22)
Previous premature infant	9 (6)
In another trial	3 (2)
From country	2 (1)
Baby been through enough	6 (47)
Baby's father not interested	2 (12)
Wants baby to be able to have what s/he needs i.e. bottle or cup, dummy or not.	12 (7)
Wanted to be able to choose group allocation	5 (3)
No reason given	8 (5)

* Could give more than one reason

4.2.2 Withdrawals

Four infants were withdrawn from the trial at the mothers' request. Two withdrew from the study immediately on finding out their treatment allocation. One assigned to Cup/No Dummy decided she wanted her baby to have a bottle as she felt that this would give her the best chance of breast feeding. Another withdrew because she was randomised to Cup/No Dummy and she wanted her baby to have a dummy. One assigned to Bottle/No Dummy withdrew two days after trial entry because she was in another trial that also required completion of forms and she stated that she wanted to enjoy her baby and not worry about returning forms. The fourth mother was randomised to Bottle/Dummy, she

stated she was having difficulty dealing with having a preterm baby and decided she did not want to be involved in any trials.

Outcomes for those who withdrew were not known, as permission was no longer granted to access case notes.

4.2.3 Non compliance

The rate of non compliance with the allocated intervention was high with a large proportion of participants introducing a dummy and/or cup as shown in Figure 4.1. The following data exclude those infants who died or were withdrawn from the study. Of the 151 infants randomised to the cup intervention 85 (56%) had a bottle introduced. 47 (31%) of the 152 infants randomised to No Dummy had a dummy introduced. Five (3%) of the 151 infants randomised to receive a dummy did not have one and one of the 152 (0.7%) infants randomised to receive a bottle had a cup introduced.

Compliance differed between the recruiting hospitals with the WCH having a higher rate of non compliance (Table 4.2 and Table 4.3)

Table 4.2 Bottle introduced, by recruiting hospital*

Non compliance	WCH n=55 n (%)	MHW n=96 n (%)	Total n=151 n (%)
Bottle introduced	36 (66)	49 (51)	85 (56)

*Excludes infants who died or withdrawn from study

Table 4.3 Dummy introduced, by recruiting hospital*

Non compliance	WCH n=51 n (%)	MHW n=101 n (%)	Total n=152 n (%)
Dummy introduced	29 (57)	18 (18)	47 (31)

*Excludes infants who died or withdrawn from study

Data on reasons for the introduction of a bottle or dummy were collected at two time points, during the hospital stay and with the three month post discharge questionnaire. The data collected during the hospital stay were accessed from the case notes or on discussion with the attending nurses or midwives. The mothers were asked at the three month post discharge question for their reasons for non compliance.

Those who were randomised to receive a dummy but did not use it were not asked to give reasons as this was an unanticipated occurrence.

Hospital data

Reasons for introducing a bottle were available for 74% (n=63) of the 85 infants randomised to cup feeds and who had a bottle introduced and for 55% (n=26) of the 47 infants randomised to No Dummy who had a dummy introduced (Table 4.4). Parents requested a bottle to be introduced in 65% of cases while it was staff initiated in 29% of cases. The main reason for a dummy being introduced was that the infant would not settle (n=13, 50%). The infant who had a cup introduced was transferred to a hospital where cup feeding was standard practice.

Table 4.4 Non compliance - reasons from hospital data.

Bottle introduced (n=63)*	**n (%)**
Error/overlooked	2 (3)
Baby unsatisfied with cup feeds/wouldn't settle	6 (10)
Parents requested	41 (65)
Staff initiated	18 (29)
Suppressed	9 (14)
To teach to suck	8 (13)
Other	3 (5)
Dummy introduced (n=26)*	
Will not settle	13 (50)
Insufficient staff time for alternate settling	1 (4)
Parents requested	14 (54)
Unknown	4 (15)

* Could give more than one reason

The mothers' responses at three months post discharge are outlined in Table 4.5. Reasons for introducing a bottle were available for 91% (n=77) of the 85 infants randomised to cup feeds and who had a bottle introduced and for 81% (n=38) of the 47 infants randomised to No Dummy who had a dummy introduced (Table 4.4).

44% (n=34) indicated that the decision to introduce a bottle was theirs with 33% (n=25) being advised by the nurse or midwife (some responded yes to both of these statements). 26% (n=20) had problems with cup feeding, this included the baby not being able to do it, spilling a lot, not satisfied with cup feeds or took too long to feed. Ten (13%) of the respondents did not like cup feeds and changed because of this. Nine (12%) of the respondents wrote that the staff refused to cup feed their infant.

A dummy was introduced mainly because the baby was unsettled without a dummy (n=14, 37%) and to teach the baby to suck (n=11, 29%).

Table 4.5 Non compliance - reasons from three month post discharge questionnaire.

Bottle introduced (n=77)*	**n (%)**
Nurse or Midwife advised	25 (33)
Doctor advised	4 (5)
My decision	34 (44)
Influenced by partner	1 (1)
Influenced by family	0
Problems with cup feeding (not satisfied, spilling, took to long, did not feed)	20 (26)
Mother didn't like cup feeds	10 (13)
Suppressed	10 (13)
Staff refused	9 (12)
To be discharged home	4 (5)
Other	10 (13)
Dummy introduced (n=38)	
Nurse or Midwife advised	6 (16)
Doctor advised	0
My decision	14 (37)
Influenced by partner	0
Influenced by family	0
Unsettled without a dummy	14 (37)
Teach my baby to suck	11 (29)
Staff introduced the dummy	5 (13)
Other	5 (13)

* Could give more than one reason

4.2.3.1 Compliance characteristics

Dummy introduced

Of the 152 infants randomised to No Dummy, 47 (31%) had a dummy introduced. The characteristics of those who did and did not comply with the No dummy group allocation are outlined in Table 4.6.

Table 4.6 Characteristics of those who did and did not comply with No Dummy allocation.

Characteristic (Total number respondents)	Continued with No Dummy (n=105 infants, 93 mothers)	Dummy introduced (n=47 infants, 39 mothers)
	n (%)	(n %)
*Maternal age (n=92/39)	30.5±5 (18-42)	30.5±6 (19-42)
<25 years	11 (12)	6 (15)
25 – 34 years	57 (62)	23 (59)
≥35 years	24 (26)	10 (26)
Twins (n=105/47)	25 (24)	17 (36)
Parity (n=93/38)		
Primiparous	34 (37)	17 (45)
Multiparous	59 (63)	21 (55)
Lives with another adult (n=92/37)	90 (98)	35 (95)
Education (n=91/38)		
Incomplete HS	25 (28)	16 (42)
Complete HS	30 (33)	13 (34)
Tertiary	36 (40)	9 (24)
Main income source (n=92/37)		
Part time work	6 (7)	0
Full time work	79 (86)	24 (65)
Benefits	7 (8)	13 (35)
Breast fed before (n=92/37)	42 (46)	19 (51)
Never	50 (54)	18 (49)
≤ 6 weeks	6 (76)	8 (22)
>6 weeks to ≤ 3 months	4 (4)	6 (16)
>3 months to ≤ 6 months	10 (11)	0
> 6 months	22 (24)	5 (14)
Hospital (n=105/47)		
WCH	22 (21)	29 (62)
MHW	83 (79)	18 (38)
Gestation at birth (n=66/85)		
<28 weeks	11 (11)	23 (49)
28 - <34 weeks	94 (90)	24 (51)

*Mean±SD (Range)

Women who complied with the No Dummy intervention were more likely to have a tertiary education with the main source of household income from full time work. Infants were more likely to be singleton, 28 weeks gestation or more at birth and to have been recruited from the MHW.

Bottle introduced

Of the 153 infants randomised to Cup feeds, 66 (44%) continued with cup and 85 (56%) of infants had a bottle introduced. The characteristics of those who did and did not comply with the cup group allocation are outlined in Table 4.7.

Table 4.7 Characteristics of those who did and did not comply with Cup allocation.

Characteristic (Total number respondents)	Continued with Cup (n=66 infants, 64 mothers)	Bottle introduced (n=85 infants, 70 mothers)
	n (%)	(n %)
*Maternal age (n=64/70)	29.4±6 (16-42)	30±6 (18-40)
<25 years	11 (17)	13 (19)
25 – 34 years	40 (63)	40 (57)
≥35 years	13 (20)	17 (24)
Twins (n=66/85)	4 (6)	30 (35)
Parity (n=64/70)		
Primiparous	40 (63)	29 (41)
Multiparous	24 (38)	41 (59)
Lives with another adult (n=64/67)	61 (95)	62 (93)
Education (n=64/66)		
Incomplete HS	15 (23)	27 (41)
Complete HS	19 (30)	23 (35)
Tertiary	30 (47)	16 (24)
Main income source (n=64/67)		
Part time work	2 (3)	2 (3)
Full time work	52 (81)	49 (73)
Benefits	10 (16)	16 (24)
Breast fed before (n=64/67)	21 (33)	29 (43)
Never	43 (67)	38 (57)
≤ 6 weeks	4 (6)	6 (9)
>6 weeks to ≤ 3 months	0	7 (11)
>3 months to ≤ 6 months	2 (3)	6 (9)
> 6 months	15 (23)	10 (15)
Hospital (n=66/85)		
WCH	19 (29)	36 (42)
MIIW	47 (71)	49 (58)
Gestation at birth (n=66/85)		
<28 weeks	7 (11)	30 (35)
28 - <34 weeks	59 (89)	55 (65)

*Mean±SD (Range)

Women who complied with the cup feeding intervention were more likely to be primiparous, tertiary educated with the main source of household income from full time work. Infants were more likely to have been singleton, 28 weeks gestation or more at birth, and to have been recruited from the MHW.

4.3 Baseline demographic and clinical characteristics

Comparisons of trial entry characteristics were undertaken to identify any imbalances at randomisation. The baseline demographic and clinical characteristics includes all infants and their mothers who were entered into the trial and randomised (Infants n=319, Mothers n=278)

4.3.1 Maternal characteristics

Table 4.8 shows that the maternal characteristics of the four groups were generally comparable after randomisation. Some baseline differences occurred between the groups; the Cup/Dummy group had the highest proportion of primiparous women and Bottle/No Dummy the lowest. The Cup/No Dummy group also had the highest proportion of women with a tertiary level of education.

Table 4.8 Maternal characteristics on trial entry

Characteristic (Total No. respondents in each group).	**Cup/ No Dummy (n=75)**	**Cup/ Dummy (n=66)**	**Bottle/ No Dummy (n=64)**	**Bottle/ Dummy (n=73)**
	n (%)	n (%)	n (%)	n (%)
Parity (n=75/66/62/73)				
Primiparous	34 (45)	40 (61)	22 (35)	36 (49)
Multiparous	41 (55)	26 (39)	40 (65)	37 (51)
*Maternal age, years (n=75/66/62/73)	31±5.4 (18-42)	28±6.0 (16-41)	30±5.5 (19-42)	29±5.9 (15-39)
<25 years	8 (11)	18 (27)	10 (16)	18 (25)
25-34 years	47 (63)	36 (55)	36 (58)	41 (56)
≥35 years	20 (27)	12 (18)	16 (26)	14 (19)
Lives with another adult (n=72/64/63/66)	70 (97)	58 (91)	60 (95)	60 (91)
Education (n=72/63/62/67)				
Incomplete High School	21 (29)	22 (35)	21 (34)	29 (43)
Complete High School	19 (26)	24 (38)	26 (42)	17 (25)
Tertiary	32 (44)	17 (27)	15 (24)	21 (31)
Main income source (n=72/63/62/67)				
Part time work	3 (4)	1 (2)	3 (5)	1 (2)
Full time work	58 (81)	46 (72)	48 (76)	50 (77)
Benefits	11 (15)	17 (27)	12 (19)	14 (22)

*Mean±SD (Range)

4.3.2 Breast feeding experience

Table 4.9 summarises the women's breast feeding intention and experience. A small number of women had not intended breast feeding their baby if they had delivered at term (n=13, 5%). They only chose to breast feed their preterm infant because of information regarding the benefits of breast milk to their preterm infant given to them by clinicians on the birth of their infant. More women in the Cup/No Dummy group had planned to breast feed for longer than six months, and the Cup/Dummy group had the greatest proportion of women with no previous breast feeding experience.

Table 4.9 Breast feeding experience on trial entry

Breast feeding (Total No. respondents in each group).	**Cup/No Dummy (n=75)**	**Cup/ Dummy (n=66)**	**Bottle/ No Dummy (64)**	**Bottle/ Dummy (n=73)**
	n (%)	n (%)	n (%)	n (%)
During pregnancy had planned to breast feed (n=72/64/63/68)	70 (97)	60 (94)	59 (94)	65 (96)
Length of time planned to breast feed (n=70/61/59/65)				
≤ 6 weeks	1 (1)	0 (0)	1 (2)	3 (5)
>6 weeks to ≤ 3 months	2 (3)	2 (3)	3 (5)	4 (6)
>3 months to ≤ 6 months	9 (13)	15 (25)	16 (27)	13 (20)
> 6 months	42 (60)	31 (51)	30 (51)	35 (52)
Don't know	16 (23)	13 (21)	9 (15)	10 (15)
Breast fed before (n=72/64/63/68)				
Yes	32 (44)	20 (31)	31 (49)	25 (37)
No	40 (56)	44 (69)	32 (51)	43 (63)
Length of time breast fed before (n=72/64/63/68)				
Never	40 (56)	44 (69)	32 (51)	43 (63)
≤ 6 weeks	5 (7)	6 (9)	9 (14)	6 (9)
>6 weeks to ≤ 3 months	6 (8)	2 (3)	5 (8)	6 (9)
>3 months to ≤ 6 months	5 (7)	3 (5)	5 (8)	7 (10)
> 6 months	16 (22)	9 (14)	12 (19)	6 (9)

4.3.3 Neonatal characteristics at birth

Two infants were part of triplets, the first triplet died at birth and these infants were therefore treated as twins. Table 4.10 shows the characteristics of the groups at birth. The Cup/Dummy group had the smallest proportion of twins. Infants in the Bottle/No Dummy group were on average approximately 150 grams heavier than infants in the other groups.

Table 4.10 Birth characteristics on trial entry

Characteristic (Total No. respondents in each group).	Cup/ No Dummy (n=89)	Cup/ Dummy (n=72)	Bottle/ No Dummy (n=73)	Bottle/ Dummy (n=85)
	n (%)	n (%)	n (%)	n (%)
Hospital recruited to (n=89/72/73/85)				
WCH	31 (35)	27 (38)	24 (33)	26 (31)
MHW	58 (65)	45 (63)	49 (67)	59 (69)
Twins	28 (31)	12 (17)	18 (25)	24 (28)
Method of delivery (n=89/72/72/84):				
Vaginal	29 (33)	26 (36)	24 (33)	23 (27)
Instrument	10 (11)	1 (1)	5 (7)	7 (8)
Caesarean, no labour	7 (8)	9 (13)	10 (14)	14 (17)
Caesarean with labour	43 (48)	36 (50)	33 (46)	40 (48)
*Birth weight, grams (n=89/72/72/85)	1325±453 (552 to 2520)	1344±488 (609 to 2560)	1508±463 (720 to 2530)	1382±469 (500 to 2580)
Gestational age at birth, weeks: (n=89/72/73/85)	29.2±2.7 (24 to 33)	29.5±2.7 (23 to 33)	30.3±2.6 (25 to 33)	29.6±2.6 (24 to 33)
<28 weeks	25 (28)	17 (24)	14 (19)	20 (24)
28 to < 34 weeks	64 (72)	55 (76)	59 (81)	65 (76)

*Mean±SD (Range)

4.3.4 Separation from WCH/MHW

Similar proportions of infants from all four groups were discharged directly home from the WCH and MHW as shown in Table 4.11. Approximately 60% of infants were transferred to a peripheral hospital for continuing care before being discharged home. During the period of the trial the MHW introduced 'Hospital in the Home' care where infants were discharged home, some still requiring some gavage feeds, and were visited daily by midwives until discharged from the program. Nineteen infants were involved in the Hospital in the Home program. For the purposes of this study these infants were treated as being transferred to a peripheral hospital while on the Hospital in the Home program, discharge home was deemed to be the date of discharge from the Hospital in the Home program. Twelve infants died during the study, one infant was transferred to a peripheral hospital and died at that hospital.

Table 4.11 Separation details*

Separation from WCH/MHW:	Cup/ No Dummy (n=87)	Cup/ Dummy (n=72)	Bottle/ No Dummy (n=72)	Bottle/ Dummy (n=84)
	n (%)	n (%)	n (%)	n (%)
Discharged directly home	35 (40)	27 (38)	23 (32)	32 (38)
Transferred to peripheral hospital	47 (54)	42 (58)	48 (67)	50 (60)
Died at WCH/MHW	5 (6)	3 (4)	1 (1)	2 (2)
Died at peripheral hospital	0	0	1	0

*excludes those who withdrew from the study

4.3.5 Neonatal clinical characteristics

The infants in all four groups required a similar amount of respiratory support as shown in Table 4.12 by need for intermittent positive pressure ventilation (IPPV) and continuous positive airway pressure (CPAP). A similar proportion of infants from all groups required home oxygen therapy. The predominant respiratory diagnosis in all groups was Hyaline Membrane Disease (HMD).

Table 4.12 Clinical characteristics*

Characteristic (Total No. respondents in each group).	**Cup/ No Dummy (n=89)**	**Cup/ Dummy (n=72)**	**Bottle/ No Dummy (n=73)**	**Bottle/ Dummy (n=85)**
	n (%)	n (%)	n (%)	n (%)
Respiratory support				
Oxygen use ≥ 1 day (n=87/71/72/85)	73 (84)	57 (80)	51 (71)	68 (80)
IPPV (n=87/72/72/85)	62 (71)	48 (67)	40 (56)	57 (67)
†Days IPPV (n=62/48/40/57)	5 (2, 19)	6 (3, 22)	3 (2, 19)	5 (2, 19)
CPAP (n=87/72/72/85)	50 (57)	44 (61)	34 (47)	48 (56)
†Days CPAP	6 (2, 16)	5 (2, 13)	3 (1, 11)	4 (2, 11)
Home oxygen (n=89/72/73/85)	11 (12)	8 (11)	4 (5)	8 (9)
Main respiratory diagnosis (n=87/72/72/85)				
HMD	60 (69)	48 (67)	40 (56)	56 (66)
Normal	11 (13)	11 (15)	15 (21)	14 (16)
Non specific	11 (13)	13 (18)	11 (15)	12 (14)
PPHN	1 (1)	0	0	0
Unknown	1 (1)	0	0	0
Apnoea	3 (4)	0	4 (6)	3 (4)
Other	0	0	2 (3)	0
Central Nervous System				
PV/IVH, any grade (n=89/72/72/85)	16 (18)	8 (11)	5 (7)	12 (14)
PVLE (n=89/72/72/85)	4 (4)	2 (3)	1 (1)	1 (1)
Necrotising enterocolitis (n=89/72/72/85)	1(1)	3 (4)	1 (1)	4 (5)

*Please refer to Abbreviations and Glossary.
†Median (25th, 75th percentile)

4.3.6 Dummy use at 48 hours of age or less.

The eligibility criteria included dummy use for less than or equal to 48 hours. This occurred in only a small proportion of the study participants and was equally distributed among the groups: Cup/No Dummy 12 of 89 (14%); Cup/Dummy 10 of 72 (14%), Bottle/No Dummy 10 of 73 (14%) and Bottle/Dummy 12 of 85 (14%).

4.3.7 Suppressed expressing before oral feeds began

Equal numbers of infants across the four groups had not commenced oral feedings when their mother stopped expressing: Cup/No Dummy 9 of 82 (11%); Cup/Dummy 8 of 69 (12%), Bottle/No Dummy 7 of 70 (10%) and Bottle/Dummy 11 of 82 (13%). These data exclude those infants who were withdrawn from the study and those who died.

4.3.8 Standard and other care

Skin-to-skin contact is standard care in both recruiting hospitals and has been shown to improve breast feeding outcomes (Whitelaw et al. 1988). This occurred equally among the groups (Table 4.13). The use of nipple shields and Maxolon was also evenly distributed in the groups (Table 4.13). These data were collected at the three month questionnaire and exclude those who died or were withdrawn from the study

Table 4.13 Standard and other care

Characteristic (Total No. respondents in each group).	**Cup/ No Dummy (n=82)**	**Cup/ Dummy (n=69)**	**Bottle/ No Dummy (n=70)**	**Bottle/ Dummy (n=82)**
	n (%)	n (%)	n (%)	n (%)
Skin-to-skin contact (63/58/51/55)				
Yes	50 (79)	44 (76)	35 (69)	47 (86)
No	13 (21)	13 (22)	15 (29)	8 (15)
Unsure	0	1 (2)	1 (2)	0
Maxolon (64/59/52/56)				
Yes	21 (33)	23 (39)	16 (31)	17 (30)
No	43 (67)	36 (61)	36 (69)	39 (70)
Nipple shield (74/64/59/65)				
Yes	18 (24)	22 (34)	19 (32)	17 (26)
No	56 (76)	42 (66)	40 (68)	48 (74)

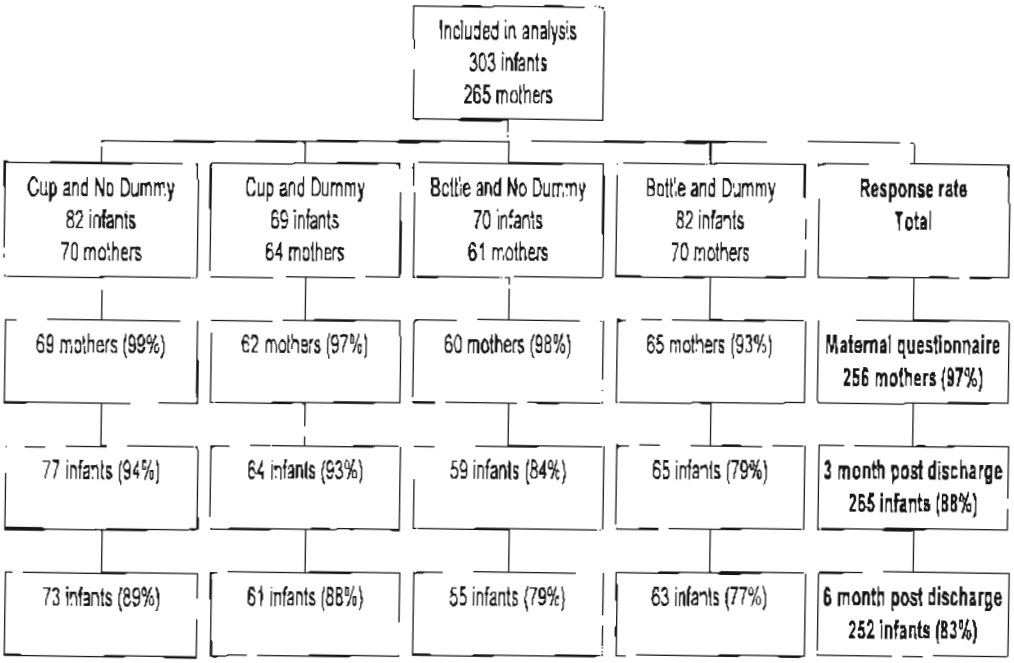
4.4 Number analysed

An intention to treat analysis was performed for the primary and secondary outcomes. The twelve infants who died were excluded from the analysis as they did not reach the primary end point of breast feeding on discharge home. The four infants who were withdrawn were also excluded from the analysis as permission was no longer granted to access their case notesAppendix X: Post-randomisation exclusion characteristics. Three hundred and three infants were therefore included in the intention to treat analysis (Figure 4.1). Three of the infants who died were twins; their surviving twin was recoded for the purposes of analysis of the primary and secondary endpoints to singleton.

All of the infants randomised, for whom data were available, were included in the survival analysis.

The response rate for each of the questionnaires is shown in Figure 4.2.

Figure 4.2 Response rate



The number of participants in each group included in each of the primary and secondary analyses is shown in Figure 4.3 and Figure 4.4.

Figure 4.3 Number analysed for each study endpoint (excluding survival analysis)

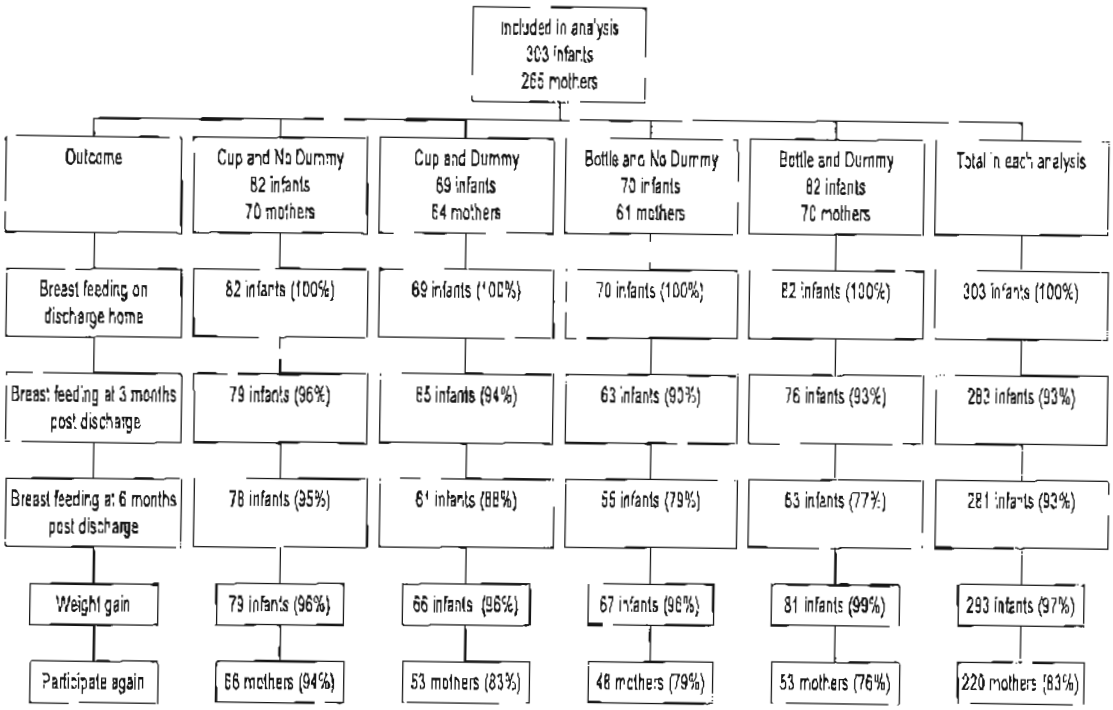
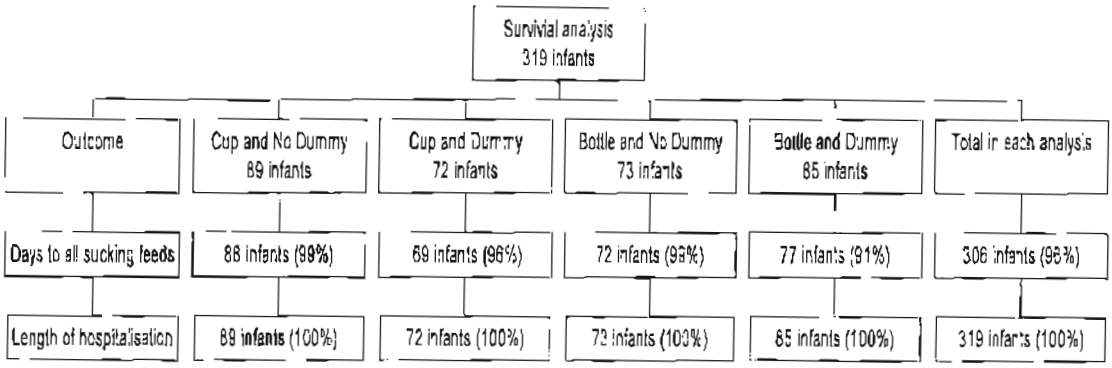


Figure 4.4 Number analysed in the survival analysis



4.5 Characteristics of infants excluded post-randomisation

The baseline demographic and clinical characteristics of the sixteen post randomisation exclusions for the primary and secondary analyses (excluding survival analysis for secondary endpoints Days to all sucking feeds and length of hospital stay) are shown in Appendix X: Post-randomisation exclusion characteristics. The infants excluded post-randomisation made up 5% of the infants randomised to the study and did not differ in any major way from those that remained in the study.

Chapter 5. Results: Primary study end points

5.1 Primary hypotheses

The clinical trial tested the following hypotheses:

1. That preterm infants who have non nutritive sucking on a dummy have a different breast feeding success rate from preterm infants who do not have dummy sucking opportunities
2. That a strategy of breast and cup feeding of growing preterm infants results in a different breast feeding success rate from a breast and bottle strategy.

5.1.1 Primary study end point

The primary study end point measures are:

1. The proportion of infants fully breast feeding on discharge home, and
2. The proportion of infants with any breast feeding (fully and partially) on discharge home

5.2 Results

Table 5.1 shows the breakdown of breast feeding according to Labbok and Krasovec's breast feeding definitions (1990).

Table 5.1 Breast feeding status on discharge home*

Breast feeding status	Cup/ No Dummy (n=82)	Cup/ Dummy (n=69)	Bottle/ No Dummy (n=70)	Bottle/ Dummy (n=82)	All groups combined (n=303)
	n (%)	n (%)	n (%)	n (%)	n (%)
Fully	48 (59)	44 (64)	31 (44)	41 (50)	164 (54)
High partial (>80%)	5 (6)	2 (3)	9 (13)	4 (5)	20 (7)
Medium partial (20% - 80%)	4 (5)	6 (9)	5 (7)	9 (11)	24 (8)
Low partial (<20%)	1 (1)	0	0	1 (1)	2 (1)
Token	2 (2)	0	2 (3)	1 (1)	5 (2)
Nil	22 (27)	17 (25)	23 (33)	26 (32)	88 (29)

*Proportions may not sum to 100% due to rounding.

To make comparisons between fully and partially breast feeding the categories of high partial, medium partial, low partial and token were collapsed into the one category of 'partially' breast feeding (Hill et al. 1994). Table 5.2 shows the breast feeding status of infants on discharge home, by randomised group, categorised into fully, partially or not

breast feeding. Altogether, 71% of infants were discharged home breast feeding (fully or partially).

Table 5.2 Breast feeding status on discharge home (any, fully, partially, not).

Breast feeding status	Cup/ No Dummy (n=82)	Cup/ Dummy (n=69)	Bottle/ No Dummy (n=70)	Bottle/ Dummy (n=82)	All groups Combined (n=303)
	n (%)	n (%)	n (%)	n (%)	n (%)
Any breast feeding	60 (73)	52 (75)	47 (67)	56 (68)	215 (71)
Fully	*48 (59)*	*44 (64)*	*31 (44)*	*41 (50)*	*164 (53)*
Partially	*12 (15)*	*8 (12)*	*16 (23)*	*15 (18)*	*52 (17)*
Not breast feeding	22 (27)	17 (25)	23 (33)	26 (32)	88 (29)

For the analyses those fully breast feeding were compared to a combined group of those partially and not breast feeding. The prevalence of any breast feeding (fully and partially combined) were compared to not breast feeding. The dependence due to inclusion of twins was accounted for by using robust variance estimates, clustering on the mother.

5.2.1 Expressed breast milk by bottle

Six women (2%) with seven infants (2%) on discharge home had chosen to feed their infants expressed breast milk by bottle. One infant was randomised to Cup/No Dummy, two to Cup/Dummy, twins to Bottle/No Dummy and two infants to Bottle/Dummy.

5.2.2 Tests for interaction effect of cup and not using a dummy

To determine if there was an interaction effect between cup use and not using a dummy a logistic regression was performed. The first analysis was done using 'fully' breast feeding versus 'partially' and 'not' breast feeding on discharge home as the outcome variable. The independent variables were the Cup groups (irrespective of dummy use) and No Dummy groups (irrespective of cup or bottle) with a multiplicative interaction term for Cup and No Dummy. The interaction was neither clinically important nor statistically significant: OR 1.01, 95% CI 0.36 to 2.79, P=0.99. It does not matter, therefore, whether a cup or bottle is used in terms of the effect not using a dummy has on the odds of an infant discharged home fully breast feeding.

In the second analysis any breast feeding versus not breast feeding was used as the outcome variable. The interaction was again neither important nor significant: OR 0.94, 95% CI 0.31 to 2.86, P=0.91.

Based on these results, further comparisons were performed on the marginal groups: Cup versus Bottle and No Dummy versus Dummy.

5.2.3 Baseline demographic and clinical characteristics No Dummy versus Dummy groups

The maternal characteristics, breast feeding experience, birth and neonatal clinical characteristics were evenly distributed between the No Dummy and Dummy groups. A difference greater than or equal to 10% in the distribution between the groups occurred for:

- Parity, where the No Dummy group had fewer primiparous women (No Dummy n=51, 39%; Dummy n=74, 55%)
- Previous breast feeding experience, where more women in the No Dummy group had breast fed before (No Dummy n=61, 47%, Dummy n=42, 33%).

5.2.4 Baseline demographic and clinical characteristics Cup versus Bottle groups

The maternal characteristics, breast feeding experience, birth and neonatal clinical characteristics were also evenly distributed between the Cup and Bottle groups. A difference greater than or equal to 10% in the distribution between the groups occurred for parity, where the Cup group had more primiparous women (Cup n=69, 52%; Bottle n=56, 43%).

5.2.5 No Dummy versus Dummy, breast feeding outcomes on discharge home

Table 5.3 shows the proportion of infants breast feeding on discharge home according to dummy use.

Table 5.3 Breast feeding prevalence by dummy use

Breast feeding status	**No Dummy (n=152)**	**Dummy (n=151)**
	n (%)	n (%)
Any breast feeding	107 (70)	108 (72)
Fully	*79 (52)*	*85 (56)*
Partially	*28 (18)*	*23 (15)*
Not breast feeding	45 (30)	43 (29)

Not using a dummy had no significant effect on the proportion of infants fully breast feeding (Table 5.4) or any breast feeding (Table 5.5) on discharge home. Infants were less

likely to be fully breast fed if they did not have a dummy but this did not reach statistical significance.

Table 5.4 Summary results No Dummy versus Dummy – 'fully' breast feeding

Primary endpoint 1	No Dummy (n=152)	Dummy (n=151)		
	n (%)	n (%)	OR (95% CI)	P Value
Fully breast feeding	79 (52)	85 (56)	0.84 (0.51 to 1.39)	0.50
Partially and Not breast feeding	73 (48)	56 (44)		

Table 5.5 Summary results No Dummy versus Dummy – 'Any' breast feeding

Primary endpoint 2	No Dummy Groups (n=152)	Dummy Groups (n=151)		
	n (%)	n (%)	OR (95% CI)	P Value
'Any' breast feeding	107 (70)	108 (72)	0.95 (0.55 to 1.65)	0.85
Not breast feeding	45 (30)	43 (28)		

5.2.6 Confounding – No dummy versus Dummy

To explore the effect of confounding, indicator variables were entered into the model where there was a 10% or greater difference in the distribution between the No Dummy or Dummy groups (parity and previous breast feeding experience) or where the indicator variables were identified a priori as predictors for breast feeding success in preterm infants (breast fed before, education and gestational age at birth). If the indicator variable changed the odds ratio by 10% or more it was retained in the model (Elwood 1998, p.157). The dependence due to inclusion of twins was accounted for by using robust variance estimates.

5.2.6.1 Confounding - outcome fully breast feeding, No Dummy versus Dummy

In Table 5.6 the adjusted odds ratio obtained from entering the confounding variables into the logistic model are shown. The percentage change from the unadjusted odds ratio of 0.84 is also shown.

Table 5.6 Effect of confounding No Dummy versus Dummy, fully breast feeding

Indicator variable	Adjusted OR	Percentage change
Primiparity	0.87	4
Breast fed before	0.82	2
Education	0.78	7
Gestational age <28 weeks	0.84	0

None of the potential confounders met the initial criteria for a 10% change in the unadjusted odds ratio therefore the unadjusted odds ratio was retained (OR 0.84, 95% CI 0.51 to 1.39, P=0.50).

5.2.6.2 Confounding - outcome any breast feeding, No dummy versus Dummy

In Table 5.7 the adjusted odds ratio obtained from entering the confounding variables into the logistic model are shown. The percentage change from the unadjusted odds ratio of 0.95 is also shown.

Table 5.7 Effect of confounding No Dummy versus Dummy, any breast feeding

Indicator variable	Adjusted OR	Percentage change
Recruiting hospital	0.94	1
Primiparity	0.97	2
Breast fed before	0.90	4
Education	0.83	13
Gestational age <28 weeks	0.95	0

Education met the criteria for a 10% change in the odds ratio and the adjusted odds ratio was retained (adjusted OR 0.83, 95% CI 0.45 to 1.50, P=0.53).

5.2.7 Breast feeding on discharge home by recruiting hospital and No Dummy versus Dummy

Exploration of breast feeding outcomes by recruiting hospital were undertaken to explore possible heterogeneity across recruiting sites as described in Chapter 3 (section 3.11.3). Although there was a positive association with fully breast feeding on discharge home for infants recruited from the WCH and randomised to the No Dummy groups (OR 1.37, 95% CI 0.59 to 3.19), and an inverse association for infants recruited from the MHW (OR 0.65, 95% CI 0.36 to 1.18), the test for interaction was not significant: OR 2.11, 95% CI 0.73 to 6.12, P=0.17. For the outcome any breast feeding the interaction was neither important nor significant: OR 1.00, 95% CI 0.32 to 3.14, P=1.00.

While the recruiting centre specific analysis raises questions about the effect of dummy use on the outcome fully breast feeding on discharge home, the a priori hypotheses did not entail a recruiting centre specific effect and the study is underpowered to detect it, the main results, therefore, will continue to be based on the overall data. (See Appendix XI: Outcomes by recruiting hospital for detail of breast feeding prevalence by recruiting hospital).

5.2.8 Outcome first research hypothesis

The first research hypothesis, that preterm infants less than 34 weeks gestation who have non nutritive sucking on a dummy have a different breast feeding success rate than preterm infants who do not have dummy sucking opportunities, is therefore rejected.

5.2.9 Cup versus Bottle, breast feeding outcomes on discharge home

Table 5.8 shows the breast feeding prevalence on discharge home according to allocation to Cup or Bottle groups.

Table 5.8 Breast feeding prevalence Cup versus Bottle

Breast feeding status	**Cup (n=151)**	**Bottle (n=152)**
	n (%)	n (%)
Any breast feeding	112 (74)	103 (68)
Fully	*92 (61)*	*72 (47)*
Partially	*20 (13)*	*31 (20)*
Not breast feeding	39 (26)	49 (32)

There is a statistically significant difference in the odds of infants discharged home fully breast feeding, with those randomised to cup feeds 73% more likely to be fully breast fed on discharge home (Table 5.9).

Table 5.9 Summary results Cup versus Bottle – 'fully' breast feeding

Primary endpoint 1	**Cup (n=151)**	**Bottle (n=152)**		
	n (%)	**n (%)**	**OR (95% CI)**	**P Value**
Fully breast feeding	92 (61)	72 (47)	1.73 (1.04 to 2.88)	0.03
Partially and Not breast feeding	59 (39)	80 (53)		

Infants were more likely to have any breast feeding if they had cup feeds, however this did not reach statistical significance (Table 5.10).

Table 5.10 Summary results Cup versus Bottle – 'any' breast feeding

Primary endpoint 2	Cup groups (n=151)	Bottle Groups (n=152)		
	n (%)	n (%)	OR (95% CI)	P Value
'Any' breast feeding	112 (74)	103 (68)	1.37 (0.78 to 2.38)	0.27
Not breast feeding	39 (26)	49 (32)		

5.2.10 Confounding - Cup versus Bottle

The effect of confounding was explored as described in section 5.2.6. There was a 10% or greater difference in the distribution between the Cup and Bottle groups for the variable parity. Previous breast feeding experience, education and gestational age at birth were identified a priori as potential confounding for breast feeding success as previously described.

5.2.10.1 Confounding – outcome fully breast feeding, Cup versus Bottle

In Table 5.11 the adjusted odds ratio obtained from entering the confounding variables into the logistic model are shown. The percentage change from the unadjusted odds ratio of 1.73 is also shown.

Table 5.11 Effect of confounding Cup versus Bottle, fully breast feeding

Indicator variable	Adjusted OR	Percentage change
Primiparity	1.70	2
Breast fed before	1.71	1
Education	1.62	6
Gestational age <28 weeks	1.88	9

Women with a tertiary education were nearly three times more likely to be fully breast feeding which was highly statistically significant (OR 2.68, 95% CI 1.36 to 5.27, P=0.004). If the infant's gestational age at birth was less than 28 weeks they were 67% less likely to be fully breast feeding on discharge home than more mature infants (OR 0.33, 95% CI 0.17 to 0.62, P=0.001).

Although none of the potential confounders met the initial criteria for a 10% change in the unadjusted odds ratio, two variables, education and gestational age, caused a relative change. Adjusting for these two variables changed the odds ratio from 1.73 to 1.78. This change was judged not important and in the interest of a parsimonious model the unadjusted odds ratio was retained (OR 1.73, 95%CI 1.04 to 2.88, P=0.03).

5.2.10.2 Confounding – outcome any breast feeding, Cup versus Bottle

In Table 5.12 the adjusted odds ratio obtained from entering the confounding variables into the logistic model are shown. The percentage change from the unadjusted odds ratio of 1.37 is also shown.

Table 5.12 Effect of confounding Cup versus Bottle, any breast feeding

Indicator variable	Adjusted OR	Percentage change
Primiparity	1.35	2
Breast fed before	1.32	4
Education	1.21	12
Gestational age <28 weeks	1.53	12

Women with a tertiary education were four times more likely to have any breast feeding on discharge home, which was highly statistically significant (OR 4.27, 95% CI 1.82 to 10.01, P=0.001). If the infant's gestational age at birth was less than 28 weeks they were 77% less likely to have any breast feeding on discharge home than more mature infants (OR 0.23, 95% CI 0.12 to 0.44, P<0.001).

Education and gestational age at birth less than 28 weeks gestation met the criteria for a 10% change in the unadjusted odds ratio. The odds ratio was reduced minimally when adjusting for these variables, therefore the unadjusted odds ratio was retained (OR 1.37, 95% CI 0.78 to 2.38, P=0.27).

5.2.11 Breast feeding on discharge home by recruiting hospital and Cup versus Bottle

The effect of Cup versus Bottle on the outcomes fully breast feeding and any breast feeding was not significantly different between the two hospitals and the primary results from the overall models stand (fully breast feeding OR 1.39, 95% CI 0.48 to 4.03, P=0.55; any breast feeding: OR 1.82, 95% CI 0.57 to 5.75, P=0.31). (See Appendix XI: Outcomes by recruiting hospital for detail).

5.2.12 Number needed to treat

The number needed to treat (NNT) is seven (95% CI 4 to 50), thus seven infants would need to be cup fed for one extra infant to be discharged home fully breast feeding.

5.2.13 Outcome second research hypothesis

The second hypothesis, that a strategy of breast and cup feeding of growing preterm infants results in a different breast feeding success rate than a breast and a bottle strategy, is supported only for those fully breast feeding on discharge home.

5.3 Summary of primary study end point results

The first research hypothesis, that preterm infants less than 34 weeks gestation who have non nutritive sucking on a dummy have a different breast feeding success rate than preterm infants who do not have dummy sucking opportunities, is not supported. Not using a dummy did not improve breast feeding outcomes.

The second research hypothesis, that a strategy of breast and cup feeding of growing preterm infants less than 34 weeks gestation results in a different breast feeding success rate than a breast and a bottle strategy, is supported for those fully breast feeding on discharge home. There was a trend to an increased prevalence of 'any' breast feeding for those randomised to cup feeds, but this did not reach significance. With the number of infants included in this trial a 14.5% increase from 68% to 82.5% could have been detected in the outcome any breast feeding. To determine if there is a statistically significant difference in the prevalence of 'any' breast feeding found in this study between Cup (74%) and Bottle (68%), a sample size of 1860 would be required.

Chapter 6. Results from the secondary study end points

6.1 Secondary study end points

The secondary study endpoints measured for the trial were:

- The proportion of infants breast feeding at three months post discharge.
- The proportion of infants breast feeding at six months post discharge.
- The number of days to reach all sucking feeds
- Duration of hospitalisation
- Weight gain from birth to discharge home
- Feelings about participation in the trial

6.1.1 Breast feeding definition for secondary study end points

For the purposes of the secondary study endpoints Labbok and Krasovec's (1990) breast feeding definitions were not used. The intent here was to determine the type of milk feeds infants were receiving (breast or formula) irrespective of whether they were receiving solids. The category of 'All breast feeds' implies that the infant's milk feeds were only breast feeds with no other types of milk given, 'partial' means that the infant's milk feeds were a combination of breast feeds and other types of milk. Data were collected on the timing of introduction of solids, however these could not be used as it became apparent that some mothers were using actual age and some corrected age and it could not be determined with confidence which was used.

6.2 Breast feeding at three months post discharge

The breast feeding prevalence at three months post discharge was calculated from responses to the self-reported questionnaire. Responses were received for 265 infants, a response rate of 88%. Non respondents who were not breast feeding on discharge home (n=18) were coded as not breast feeding, giving data for 93% (n=283) of infants.

Overall 39% of infants were being breast fed at three months post discharge (Table 6.1).

Table 6.1 Milk feeds at three months post discharge*

Milk feeds at 3 months post discharge	Cup/ No Dummy (n=79)	Cup/ Dummy (n=65)	Bottle/ No Dummy (n=63)	Bottle/ Dummy (n=76)	All groups Combined (n=283)
	n (%)	n (%)	n (%)	n (%)	n (%)
Any breast feeding	34 (43)	27 (42)	24 (38)	26 (34)	111 (39)
All breast feeds	*25 (32)*	*18 (28)*	*19 (30)*	*16 (21)*	*78 (28)*
Partial	*9 (11)*	*9 (14)*	*5 (8)*	*10 (13)*	*33 (12)*
Not breast feeding	45 (57)	38 (59)	39 (62)	50 (66)	172 (61)

*Proportions may not sum to 100 due to rounding.

6.2.1 No Dummy versus Dummy at three months post discharge

The breast feeding prevalence by dummy groups are presented in Table 6.2.

Table 6.2 Breast feeding prevalence at 3 months, by dummy use

Milk feeds at 3 months post discharge	No Dummy (n=142)	Dummy (n=141)
	n (%)	n (%)
Any breast feeding	58 (41)	53 (38)
All breast feeds	*44 (31)*	*34 (24)*
Partial	*14 (10)*	*19 (14)*
Not breast feeding	84 (59)	88 (62)

The odds ratio for milk feeds being all breast feeds at three months post discharge comparing those randomised to No Dummy and those randomised to Dummy was OR 1.41, 95% CI 0.80 to 2.50, P=0.24. Adjusting for confounding by previous breast feeding experience, education and gestational age at birth, made minimal change to the odds ratio. Parity caused a 12% increase in the odds ratio from 1.41 to 1.58 and the adjusted odds ratio was retained (adjusted OR 1.58, 95% CI 0.89 to 2.78, P=0.12).

The odds ratio for any (all and partially combined) breast feeds at three months post discharge comparing those randomised to No Dummy and those randomised to Dummy was OR 1.15, 95% CI 0.67 to 1.95, P=0.62. When adjusting for confounding by parity, previous breast feeding experience and gestational age at birth, there was minimal change to the odds ratio. Education caused a 14% decrease in the odds ratio from 1.15 to 0.99 and the adjusted odds ratio was retained (adjusted OR 0.99, 95% CI 0.56 to 1.77, P=0.98).

6.2.1.1 Dummy use at three months post discharge

Women were asked at the three month questionnaire whether their infant/s were using a dummy now. Responses were received from 230 (76%) (Table 6.3). Approximately 60%

of those randomised to No Dummy and those randomised to Dummy were using a dummy at three months post discharge.

Table 6.3 Dummy use at three months post discharge

Dummy use at 3 months post discharge	No Dummy (n=117)	Dummy (n=113)	Total (n=230)
	n (%)	n (%)	n (%)
Do not use a dummy	47 (40)	49 (43)	96 (42)
Use a dummy	70 (60)	64 (57)	134 (58)

6.2.2 Cup versus Bottle at three months post discharge

Table 6.4 shows the breast feeding prevalence by Cup or Bottle groups at three months post discharge.

Table 6.4 Breast feeding prevalence at 3 months, Cup versus Bottle

Milk feeds at 3 months post discharge	Cup (n=144)	Bottle (n=139)
	n (%)	n (%)
Any breast feeding	61 (42)	50 (36)
All breast feeds	*43 (30)*	*35 (25)*
Partially	*18 (13)*	*15 (11)*
Not breast feeding	83 (58)	89 (64)

The odds ratio for milk feeds being all breast feeds at three months post discharge for those randomised to the Cup groups versus Bottle groups was 1.27, 95% CI 0.72 to 2.33, P=0.42. The milk feeds of infants randomised to the Cup groups were 27% more likely to be all breast feeds at three months post discharge, but this did not reach statistical significance. Adjusting for confounding (parity, previous breast feeding experience, education and gestational age at birth) made minimal change to the odds ratio and the unadjusted odds ratio was retained.

The odds ratio for any breast feeding (all and partially combined) at three months post discharge for those randomised to the Cup groups was 1.31, 95% CI 0.77 to 2.23, P=0.33. Adjusting for confounding (parity, previous breast feeding experience, education and gestational age at birth) caused minimal change in the odds ratio and the unadjusted odds ratio was retained.

6.2.3 Reasons for stopping breast feeding by three months post discharge

At the three month questionnaire women were asked for all reason/s for stopping expressing or breast feeding. A different set of questions was used for those who stopped expressing before they started breast feeding, however this caused confusion for some respondents who answered parts of both questions. The questions were similar and were therefore combined. Of the 149 mothers with 172 infants not breast feeding at three months, responses were received from 132 mothers with 153 infants, a response rate of 89%.

The main reasons given for stopping breast feeding or expressing were insufficient milk supply (n=70, 60%), and that their baby took the bottle better (n=33, 25%), (Table 6.5).

Table 6.5 Reasons for stopping breast feeding/expressing by 3 months

Reason	Cup (n=68 mothers)	Bottle (n=64 mothers)	Total (n=132 mothers)
	n (%)	n (%)	n (%)
Maternal factors			
Life style			
Difficult to fit in expressing with other demands	7 (10)	6 (9)	13 (10)
Didn't like expressing	3 (4)	2 (3)	5 (4)
Went back to work	1 (2)	3 (5)	4 (3)
Wanted to express only while baby sick	2 (3)	1 (2)	3 (3)
Didn't like breast feeding	0	2 (3)	2 (3)
Did not really want to breast feed	0	3 (5)	3 (2)
Wanted to be able to sleep longer	1 (2)	2 (3)	3 (2)
Felt embarrassed expressing	0	0	0
Difficult to express at workplace (time/facilities)	0	0	0
Medical reason			
Had a medical reason	2 (3)	4 (6)	6 (5)
Doctor advised to stop	1 (5)	4 (6)	5 (4)
Physical			
*Insufficient milk	47 (69)	32 (50)	70 (60)
Thought baby wasn't getting enough	12 (18)	9 (14)	21 (16)
Wanted to make sure my baby got enough	7 (10)	10 (16)	17 (13)
Found expressing difficult	5 (7)	2 (3)	7 (5)
Sore nipples	0	5 (8)	5 (4)
Didn't feel milk was good enough	3 (4)	2 (3)	5 (4)
Infant factors			
Took the bottle better	15 (22)	18 (28)	33 (25)
Baby fussy during breast feeding	17 (25)	6 (9)	23 (17)
Baby refused the breast	8 (12)	10 (16)	18 (14)
Baby fussy after breast feeding	12 (18)	3 (5)	15 (11)
Baby had a weak suck	9 (13)	6 (9)	15 (11)
Breast fed too frequently	6 (9)	7 (11)	13 (10)
Poor weight gain	3 (4)	4 (6)	7 (5)
Baby sleepy at the breast	2 (3)	1 (2)	3 (2)

*Combination of questions "my milk supply did not increase enough to meet my baby's needs" and "I didn't feel I had enough milk"

6.3 Breast feeding at six months post discharge

Breast feeding status at six months post discharge was collected by questionnaire. Responses were received for 252 infants, a response rate of 83%. Non respondents who were not breast feeding on discharge home (n=18) or at three months post discharge (n=11) were coded as not breast feeding, giving data for 93% (n=281) of infants.

Breast feeding prevalence at six months post discharge according to randomisation is presented in Table 6.6. Overall 27% of infants were being breast fed at six months post discharge.

Table 6.6 Breast feeding prevalence six months post discharge*

Milk feeds at 6 months post discharge	Cup & No Dummy (n=78)	Cup & Dummy (n=64)	Bottle & No Dummy (n=63)	Bottle & Dummy (n=76)	All groups Combined (n=281)
	n (%)	n (%)	n (%)	n (%)	n (%)
Any breast feeding	27 (35)	17 (27)	16 (25)	17 (22)	77 (27)
All breast feeds	*24 (31)*	*12 (19)*	*10 (16)*	*11 (15)*	*57 (20)*
Partial	*3 (4)*	*5 (8)*	*6 (10)*	*6 (8)*	*20 (7)*
Not breast feeding	51 (65)	47 (73)	47 (75)	59 (78)	204 (73)

*Proportions may not sum to total due to rounding.

6.3.1 No Dummy versus Dummy at six months post discharge

The breast feeding prevalence by dummy groups is presented in Table 6.7.

Table 6.7 Breast feeding prevalence by dummy use at six months post discharge

Milk feeds at 6 months post discharge	No Dummy (n=141)	Dummy (n=140)
	n (%)	n (%)
Any breast feeding	43 (30)	34 (24)
All breast feeds	*34 (24)*	*23 (16)*
Partially	*9 (6)*	*11 (8)*
Not breast feeding	98 (70)	106 (76)

The odds ratio for milk feeds being all breast feeds at six months post discharge comparing those randomised to No Dummy with those randomised to Dummy was: OR 1.62, 95% CI 0.85 to 3.07, P=0.14. Adjusting for confounding (parity, previous breast feeding experience, education and gestational age at birth) caused minimal change to the odds ratio and the unadjusted odds ratio was retained.

The odds ratio for any breast feeding (all and partially combined) at six months post discharge for those randomised to No Dummy was 1.37, 95% CI 0.77 to 2.44, P=0.29. Adjusting for confounding (parity, previous breast feeding experience and gestational age at birth) caused minimal change to the odds ratio. Education caused a 10% decrease in the odds ratio from 1.37 to 1.23 and therefore the adjusted odds ratio was retained (adjusted OR 1.23, 95% CI 0.66 to 2.30, P=0.51).

6.3.1.1 Dummy use at six months post discharge

Women were asked at the six month questionnaire whether they were using a dummy. Responses were received from 237 (78%) (Table 6.8). Approximately half of those

randomised to No Dummy and those randomised to Dummy were using a dummy at six months post discharge.

Table 6.8 Dummy use at six months post discharge

Dummy use at 3 months post discharge	No Dummy (n=121)	Dummy (n=116)	Total (n=237)
	n (%)	n (%)	n (%)
Do not use a dummy	60 (50)	61 (53)	121 (51)
Use a dummy	61 (50)	55 (47)	116 (49)

6.3.2 Cup versus Bottle at six months post discharge

Table 6.9 shows the breast feeding prevalence by Cup or Bottle groups at six months post discharge.

Table 6.9 Breast feeding prevalence by Cup or Bottle use at six months post discharge

Milk feeds at 6 months post discharge	Cup (n=142)	Bottle (n=139)
	n (%)	n (%)
Any breast feeding	44 (31)	33 (24)
All breast feeds	*36 (25)*	*21 (15)*
Partially	*8 (6)*	*12 (9)*
Not breast feeding	98 (69)	106 (76)

The odds ratio for milk feeds being all breast feeds at six months post discharge for those randomised to the Cup groups was 1.91, 95% CI 0.99 to 3.67, P=0.05. The milk feeds of infants randomised to the Cup groups were 91% more likely to be all breast feeds at six months post discharge, which was just on the margin of statistical significance at the 5% level. Adjusting for confounding (parity, previous breast feeding experience, education, gestational age at birth less than 28 weeks) made minimal change to the odds ratio, therefore the unadjusted model was retained.

The odds ratio for any breast feeding (all and partially combined) at six months for those randomised to the Cup groups was 1.44, 95% CI 0.81 to 2.57, P=0.22. Adjusting for confounding (parity, previous breast feeding experience, education, gestational age at birth less than 28 weeks) made minimal change to the odds ratio, therefore the unadjusted model was retained.

6.3.3 Reasons for stopping by 6 months post discharge

The reasons for stopping breast feeding were sought from those who stopped between three and six months post discharge. Of the 99 mothers with 111 infants breast feeding at three months, data were available for 97 mothers with 109 infants. 26 mothers with 32 infants had stopped breast feeding between three and six months post discharge, reasons for stopping breast feeding were completed by 24 mothers with 30 infants. Respondents could indicate more than one reason.

The main reasons given for stopping breast feeding between three and six months were that the mother felt it was time to wean (n=8, 33%) and that they wanted to make sure their baby got enough milk (n=6, 25%), (Table 6.10).

Table 6.10 Reasons for stopping breast feeding between 3 and 6 months

Reason	**Cup (n=11 mothers)**	**Bottle (n=13 mothers)**	**Total (n=24 mothers)**
	n (%)	n (%)	n (%)
Maternal factors			
Life style			
Thought it was time to wean	4 (36)	4 (31)	8 (33)
Breast fed for as long as had planned	1 (9)	2 (15)	3 (13)
Wanted to be able to sleep longer	1 (9)	0	1 (4)
Went back to work	0	0	0
Difficult to express at workplace (time/facilities)	0	0	0
Medical reason			
Had a medical reason	2 (18)	2 (15)	4 (17)
Doctor advised to stop	0	2 (15)	2 (8)
Physical			
Wanted to make sure my baby got enough	2 (18)	4 (31)	6 (25)
Didn't feel milk was good enough	1 (9)	1 (8)	2 (8)
Thought baby wasn't getting enough	2 (18)	0	2 (8)
Sore nipples	0	1 (8)	1 (4)
Didn't think had enough milk any more	1 (9)	0	1 (4)
Infant factors			
Baby fussy after breast feeding	2 (18)	2 (15)	4 (17)
Poor weight gain	1 (9)	2 (15)	3 (13)
Baby weaned her/himself	1 (9)	2(15)	3 (13)
Baby fussy during breast feeding	1 (9)	1 (8)	2 (8)
Breast fed too frequently	0	2 (15)	2 (8)
Took the bottle better	0	0	0

6.3.4 Breast feeding duration

Figure 6.1 depicts the breast feeding prevalence for any breast feeding and fully breast feeding at the three time points studied, for those randomised to no dummy or dummy.

There was a trend for little difference in the prevalence of any or fully breast feeding on discharge home, but an increased prevalence for both outcomes, for those randomised to No Dummy, at three and six months post discharge.

Figure 6.1 Breast feeding duration No dummy versus Dummy

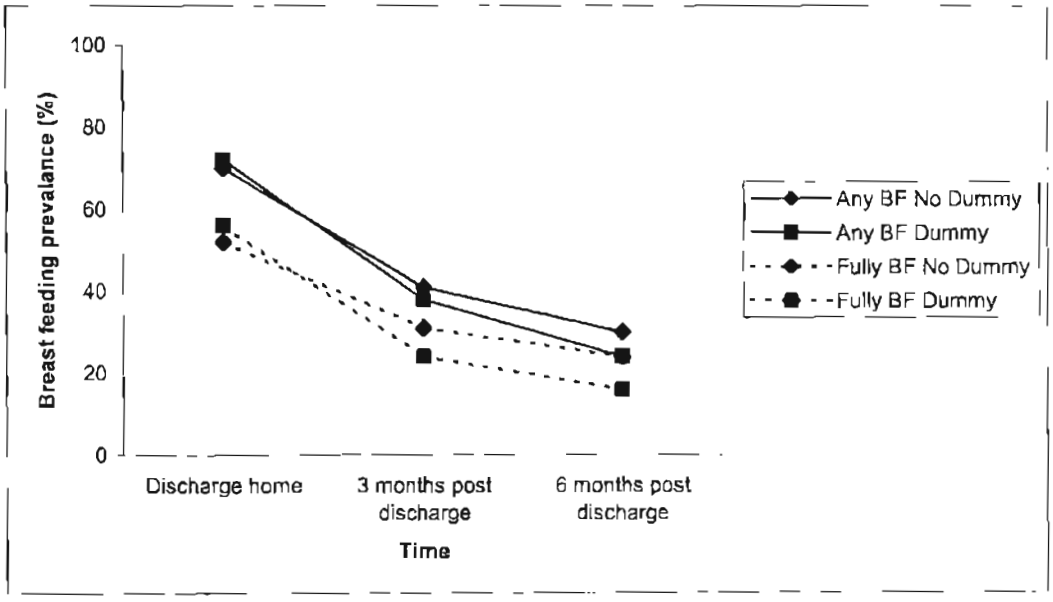
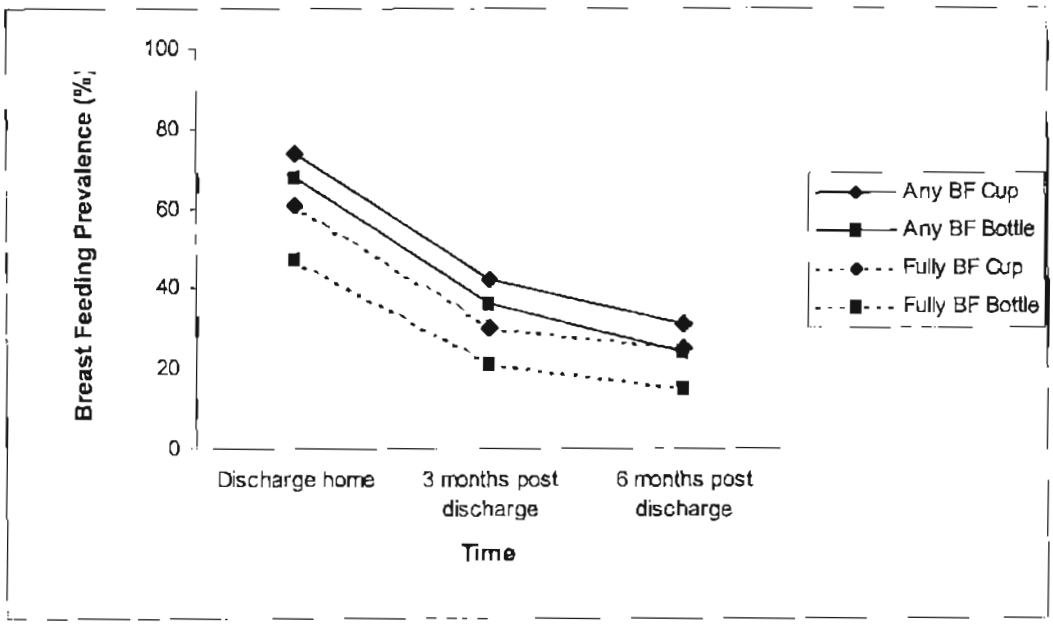


Figure 6.2 depicts the breast feeding prevalence for any breast feeding and fully breast feeding at the three time points studied, for those randomised to cup or bottle. There was a trend for an increased prevalence of any and fully breast feeding for those randomised to cup feeds at all time points, discharge home and three and six months post discharge.

Figure 6.2 Breast feeding duration Cup versus Bottle



Women who were no longer breast feeding were asked to indicate the number of months they had breast fed (or expressed), calculated from the birth of their baby. Of the 303 infants in the study, 77 were still breast feeding at six months post discharge; data were available for 203 (90%) of the 226 who had stopped breast feeding (Table 6.11).

Table 6.11 Number of months breast fed

Months breast fed	Cup (n=98)	Bottle (n=105)	Total (n=203)
	n (%)	n (%)	n (%)
< 1 month	14 (14)	19 (18)	33 (16)
1 month - < 2 months	19 (19)	33 (31)	52 (26)
2 month - < 3 months	17 (17)	22 (21)	39 (19)
3 month - < 4 months	13 (13)	8 (8)	21 (10)
4 month - < 5 months	15 (15)	6 (6)	21 (10)
5 month - < 6 months	6 (6)	8 (8)	14 (7)
6 month - < 7 months	11 (11)	7 (7)	18 (9)
7 month - < 8 months	1 (1)	2 (2)	3 (2)
8 month - < 9 months	2 (2)	0	2 (1)

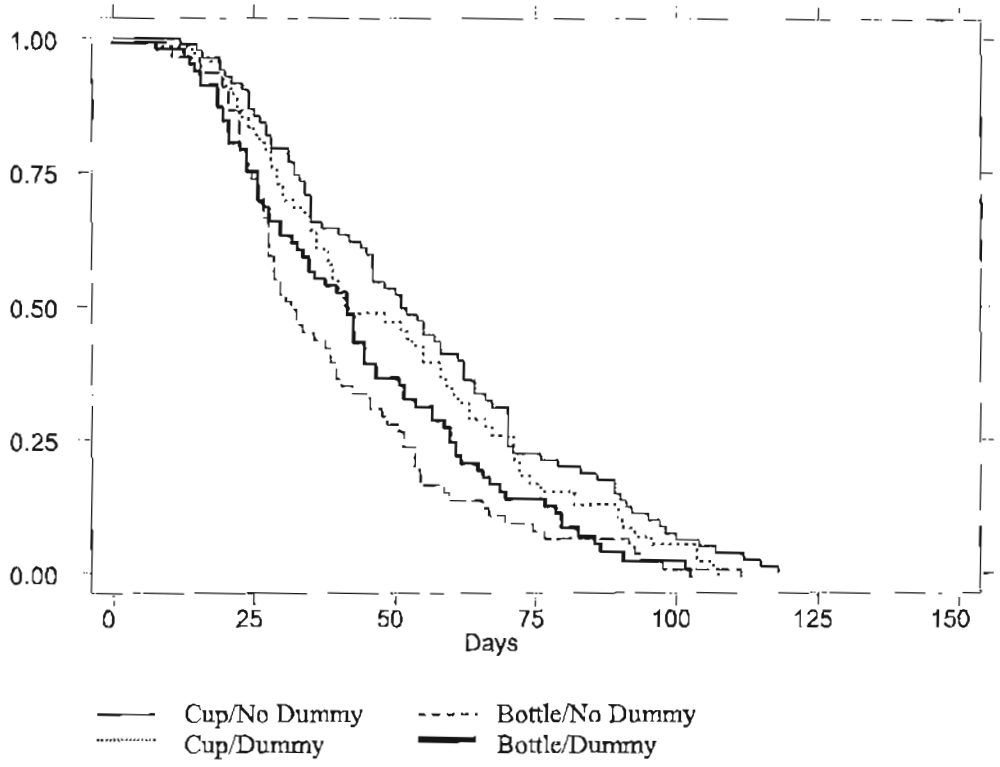
Sixty per cent of infants had stopped breast feeding by less than three months of age. This is in contrast to the Australian term infant population where 37% had stopped breast feeding by three months of age (Donath and Amir 2000). It is important to note that for some of the very preterm infants who are discharged at around term equivalent they are already several months old. For example an infant born at 24 weeks gestation and discharged home at 38 weeks post menstrual age is already 3½ months old, at three months post discharge they are 6½ months of age. But nutritionally and developmentally these infants are recalculated to corrected age, the age they would be if born at term. However from the mother's perspective she has been expressing and breast feeding for over six months.

6.4 Days to all sucking feeds

The number of days to all sucking feeds was calculated as the number of days from birth until the day of the final gavage tube feed. Cox proportional hazard models were used to estimate hazard ratios for the interventions. The dependence due to inclusion of twins was accounted for by using robust variance estimates, clustering on the mother. Data were missing for 13 infants; infants who were withdrawn and those who died were included in the survival analysis, censoring at the time of last available data, n=306.

Figure 6.3 depicts the Kaplan-Meier survival curves for the four randomised groups. Those randomised to Cup/No Dummy took the longest to reach all sucking feeds, and Bottle/No Dummy the least.

Figure 6.3 Kaplan-Meier survival estimates days to all sucking feeds, by randomised group



The summary statistics for each group are presented in Table 6.12.

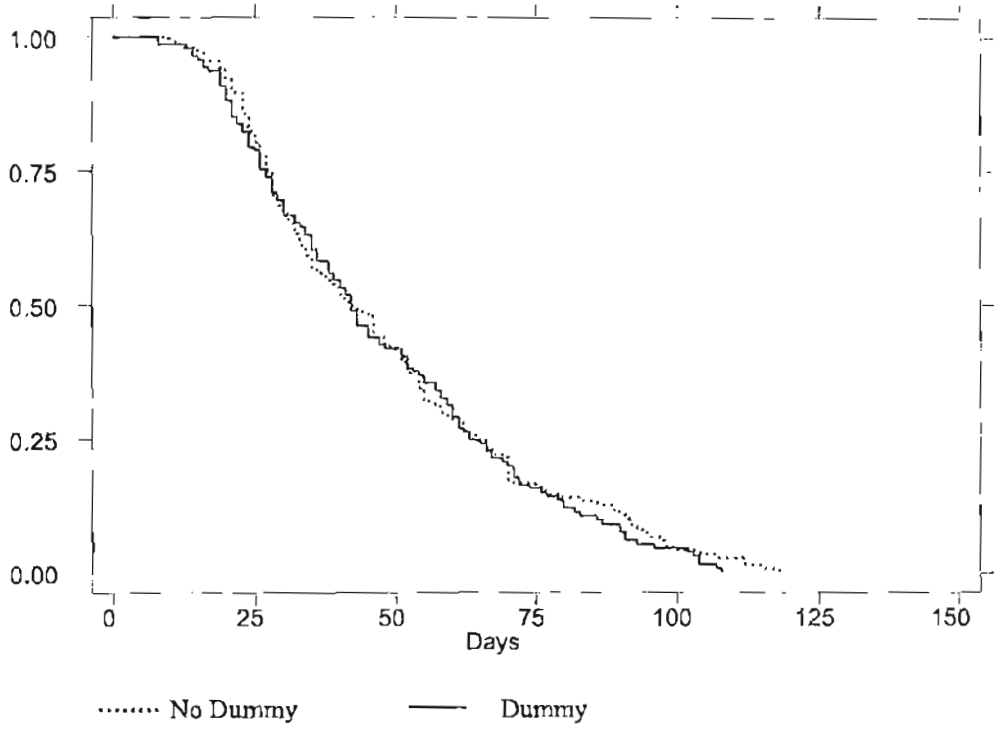
Table 6.12 Number of days to all sucking feeds, summary statistics by group randomised.

Days to all sucking feed	Cup/ No Dummy (n=88)	Cup/ Dummy (n=69)	Bottle/ No Dummy (n=72)	Bottle/ Dummy (n=77)	All groups (n=306)
Median (days)	51	42	33	42	42
Interquartile range	32-70	29-71	25-52	26-60	27-64

6.4.1 No Dummy versus Dummy

The Kaplan-Meier survival curves for the number of days taken to reach all sucking feeds analysed by allocation to No Dummy (n=160) versus Dummy (n=146) are shown in Figure 6.4.

Figure 6.4 Kaplan-Meier survival estimates days to all sucking feeds, by dummy allocation



There was no significant difference in the number of days it took to reach all sucking feeds between those randomised to No Dummy and those randomised to Dummy (HR 0.94, 95% CI 0.73 to 1.20, P=0.61). The summary statistics for No Dummy versus Dummy allocation are presented in Table 6.13.

Table 6.13 Number of days to all sucking feeds, summary statistics: No Dummy versus Dummy

Days to all sucking feed	No Dummy (n=160)	Dummy (n=146)
	days (95% CI)	days (95% CI)
25th percentile	28 (25 to 30)	27 (24 to 30)
50th percentile	42 (35 to 49)	42 (36 to 48)
75th percentile	64 (55 to 70)	63 (59 to 71)

6.4.2 Confounding – No Dummy versus Dummy

To explore the effect of confounding, indicator variables were entered into the model where there was a 10% or greater difference in the distribution between the No Dummy or Dummy groups (parity, previous breast feeding experience). Gestational age at birth is a known predictor for time to reach all sucking feeds and was also entered into the model. If the indicator variable changed the hazard ratio by 10% or more it was retained in the model. The dependence due to inclusion of twins was accounted for by using robust variance estimates.

In Table 6.14 the adjusted hazard ratios obtained from entering the confounding variables into the Cox proportional hazards model are shown. The percentage change from the unadjusted hazard ratio of 0.94 is also shown.

Table 6.14 Effect of confounding No Dummy versus Dummy, days to all sucking feeds

Indicator variable	Adjusted HR	Percentage change
Primiparity	0.93	1
Breast fed before	0.93	1
Gestational age <28 weeks	0.97	3

Infants who are more preterm at birth take longer to mature, therefore longer to reach all sucking feeds, gestational age at birth therefore is a potential confounding variable. There were a similar proportion of infants included in the survival analysis who were less than 28 weeks gestational age at birth randomised to No Dummy (n=37, 23%) and Dummy (n=32, 22%). Figure 6.5 shows the Kaplan-Meier survival curves for the number of days to reach all sucking feeds for infants with gestational age at birth less than 28 weeks. The median number of days to reach all sucking feeds for those randomised to the No Dummy groups was three days longer than for those randomised to the Dummy groups (Table 6.15), but this difference was not statistically significant (HR 0.73, 95% CI 0.44 to 1.23, P=0.24).

Figure 6.5 Kaplan-Meier survival estimates days to all sucking feeds, by No Dummy or Dummy allocation, for gestational age at birth less than 28 weeks.

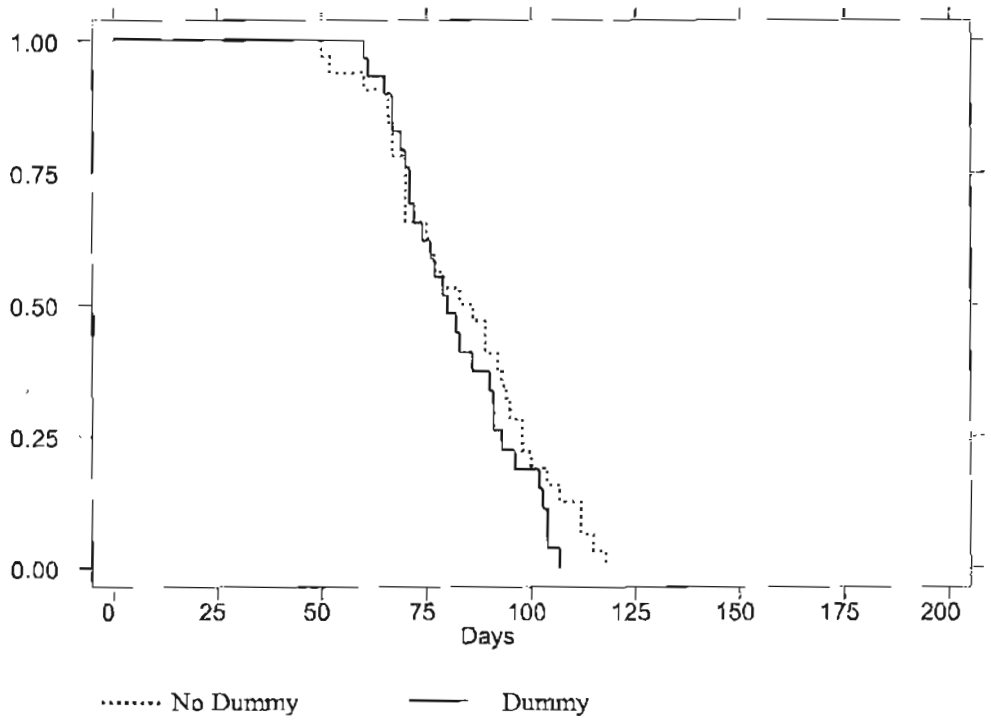


Table 6.15 Number of days to all sucking feeds, summary statistics: No Dummy versus Dummy, gestational age at birth less than 28 weeks

Days to all sucking feed	No Dummy (n=32)	Dummy (n=37)
	days (95% CI)	days (95% CI)
25th percentile	70 (60 to 76)	71 (65 to 76)
50th percentile	83 (71 to 91)	80 (70 to 94)
75th percentile	98 (83 to 104)	93 (89 to 112)

Figure 6.6 shows the Kaplan-Meier survival curves for the number of days to reach all sucking feeds for infants with gestational age at birth 28 to 34 weeks. There remained no statistically significant difference in the time taken to reach all sucking feeds (HR 1.01, 95% CI 0.76 to 1.34, P=0.94). The median number of days to reach all sucking feeds for those randomised to the No Dummy groups was two days longer than for those randomised to the Dummy groups (Table 6.16).

Figure 6.6 Kaplan-Meier survival estimates days to all sucking feeds, by No Dummy or Dummy allocation, for gestational age greater than or equal to 28 weeks and less than 34 weeks.

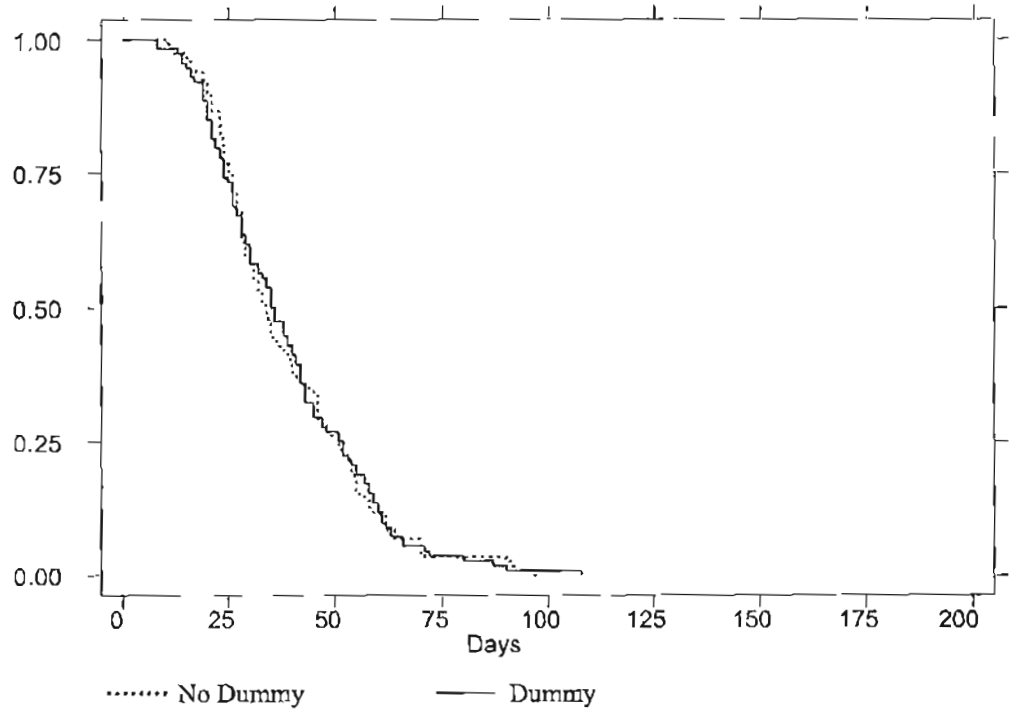


Table 6.16 Number of days to all sucking feeds, summary statistics: No Dummy versus Dummy, gestational age at birth greater than or equal to 28 weeks to less than 34 weeks

Days to all sucking feed	No Dummy (n=123)	Dummy (n=114)
	days (95% CI)	days (95% CI)
25th percentile	25 (23 to 28)	24 (21 to 27)
50th percentile	34 (30 to 39)	36 (30 to 41)
75th percentile	51 (46 to 55)	52 (43 to 57)

When infants less than 28 weeks gestational age at birth were entered into the model this caused a minimal increase in the hazard ratio of 3% from 0.94 to 0.97 and therefore was removed from the model.

None of the potential confounding variables met the criteria for a 10% change in the relative hazard, therefore the unadjusted hazard ratio was retained (HR 0.94, 95%CI 0.73 to 1.20, P=0.61).

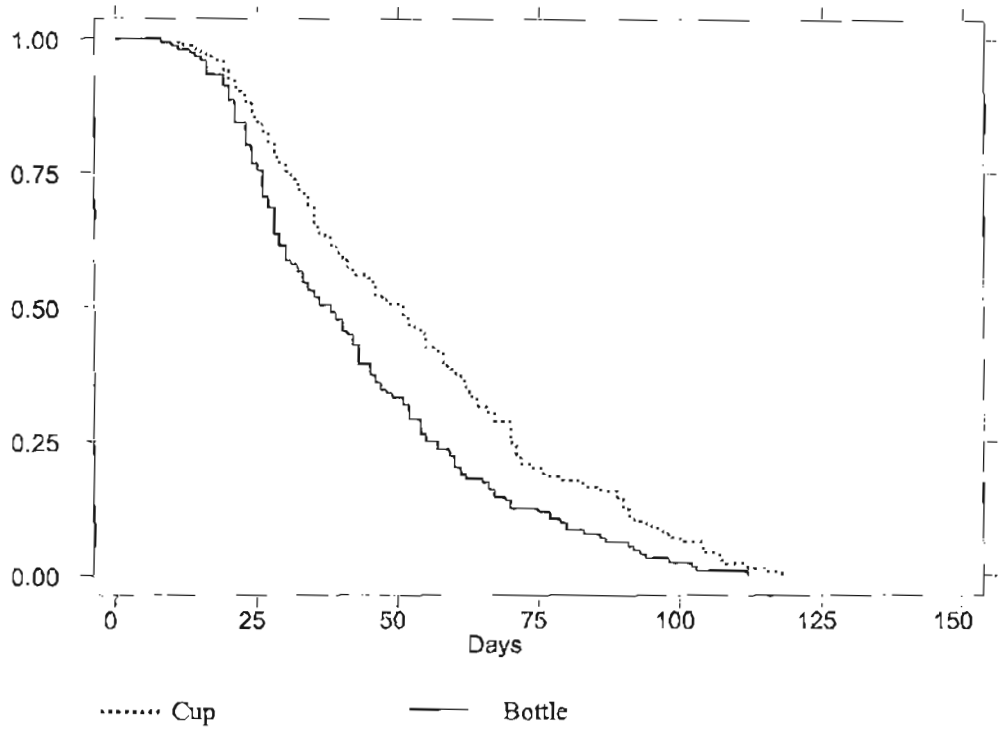
6.4.3 Days to all sucking feeds by recruiting hospital and No Dummy versus Dummy

Exploration of the outcome 'days to all sucking feeds' was undertaken by recruiting hospital to explore heterogeneity across recruiting sites. The effect of dummy use on the outcome 'days to all sucking feeds' did not differ significantly between the two recruiting hospitals and the primary results from the overall models stand (HR 1.11, 95% CI 0.68 to 1.80, P=0.69). See Appendix XI: Outcomes by recruiting hospital for more detail.

6.4.4 Cup versus Bottle

The Kaplan-Meier survival curves of the number of days taken to reach all sucking feeds according to Cup versus Bottle allocation are shown in Figure 6.7.

Figure 6.7 Kaplan-Meier survival estimates days to all sucking feeds, by Cup or Bottle allocation



The risk of taking longer to reach all sucking feeds is increased in those randomised to cup feeds (HR 1.50, 95% CI to 1.16 to 1.94, P=0.002). The summary statistics for Cup versus Bottle allocation are presented in Table 6.17. When comparing the median number of days, those randomised to receive cup feeds took 12 days longer to reach all sucking feeds than those randomised to receive bottle feeds.

Table 6.17 Number of days to all sucking feeds, summary statistics: Cup versus Bottle

Days to all sucking feed	Cup (n=157)	Bottle (n=149)
	days (95% CI)	days (95% CI)
25th percentile	31 (27 to 35)	26 (23 to 28)
50th percentile	50 (41 to 57)	38 (31 to 43)
75th percentile	70 (64 to 79)	55 (51 to 62)

6.4.5 Confounding – Cup versus Bottle

The effect of potential confounding variables on the outcome number of days to reach all sucking feeds in the Cup (n=157) versus Bottle (n=149) groups was explored as described earlier (see section 6.4.2). There was a 10% or greater difference in the distribution between the Cup or Bottle groups for the variable parity; gestational age at birth is a known predictor of time to reach all sucking feed and was also entered into the model.

In Table 6.18 the adjusted hazard ratios obtained from entering the confounding variables into the Cox proportional hazards model are shown. The percentage change from the unadjusted hazard ratio of 1.50 is also shown.

Table 6.18 Effect of confounding Cup versus Bottle, days to all sucking feeds

Indicator variable	Adjusted HR	Percentage change
Primiparity	1.50	0
Gestational age <28 weeks	1.76	17

Adding parity to the model did not change the hazard ratio and was removed from the model. Infants who are more premature at birth take longer to mature, therefore longer to reach all sucking feeds. There was a similar proportion of infants allocated to Cup with gestational age at birth less than 28 weeks (Cup n=39, 25%; Bottle n=30, 20%). Figure 6.8 shows the Kaplan-Meier survival curves for the number of days to reach all sucking feeds for infants with gestational age at birth less than 28 weeks. The median number of days to reach all sucking feeds for those randomised to cup feeds is nine days longer than for those randomised to bottle feeds (Table 6.19). The risk of taking longer to reach all sucking feeds for those randomised to Cup feeds and who are gestational age at birth less than 28 weeks now nears statistical significance (HR 1.62, 95% CI 0.93 to 2.82, P=0.09).

Figure 6.8 Kaplan-Meier survival estimates days to all sucking feeds, by cup or bottle allocation, for gestational age at birth less than 28 weeks.

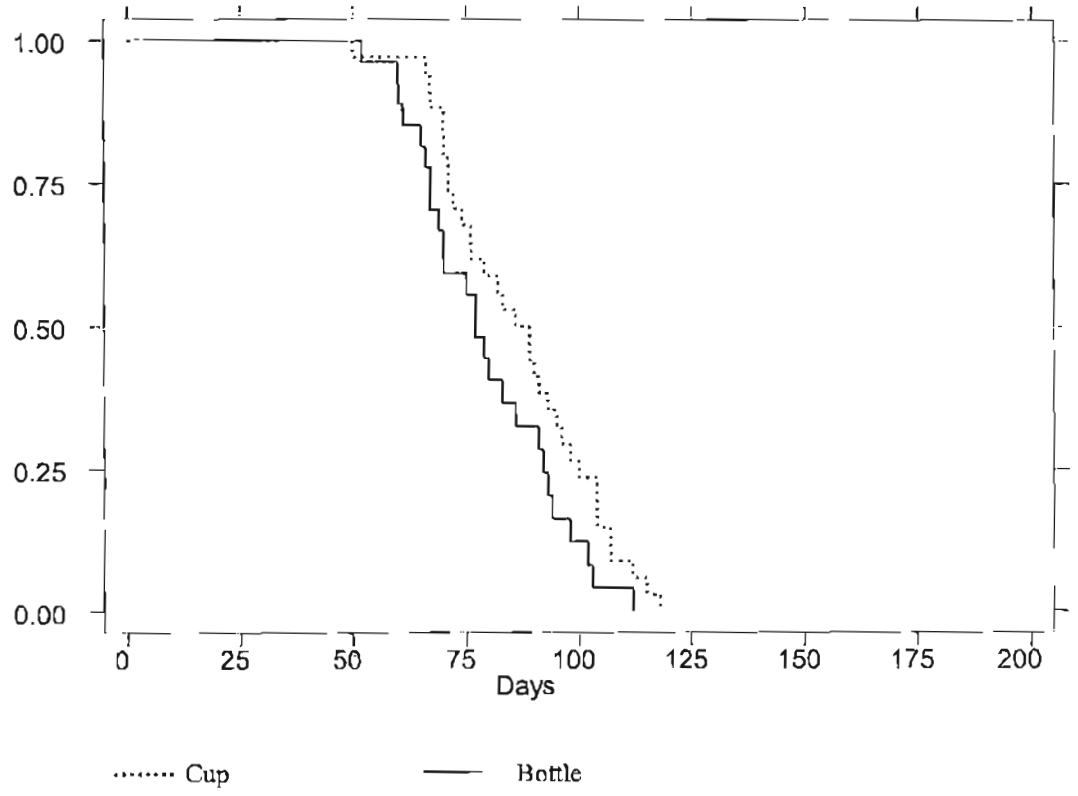


Table 6.19 Number of days to all sucking feeds, summary statistics: Cup versus Bottle, gestational age at birth less than 28 weeks

Days to all sucking feed	**Cup (n=39)**	**Bottle (n=30)**
	days (95% CI)	days (95% CI)
25th percentile	71 (67 to 79)	67 (60 to 70)
50th percentile	86 (74 to 95)	77 (67 to 91)
75th percentile	100 (90 to 109)	92 (80 to 102)

Figure 6.9 shows the Kaplan-Meier survival curves for the number of days to reach all sucking feeds for infants with gestational age at birth 28 to 34 weeks. The median number of days to reach all sucking feeds for those randomised to cup feeds is eight days longer than for those randomised to bottle feeds (Table 6.20). The risk of taking longer to reach all sucking feeds for those randomised to Cup feeds and who are gestational age at birth 28 to less than 34 weeks remains highly significantly increased (HR 1.67, 95% CI 1.26 to 2.21, P <0.001).

Figure 6.9 Kaplan-Meier survival estimates days to all sucking feeds, by cup or bottle allocation, for gestational age greater than or equal to 28 weeks and less than 34 weeks.

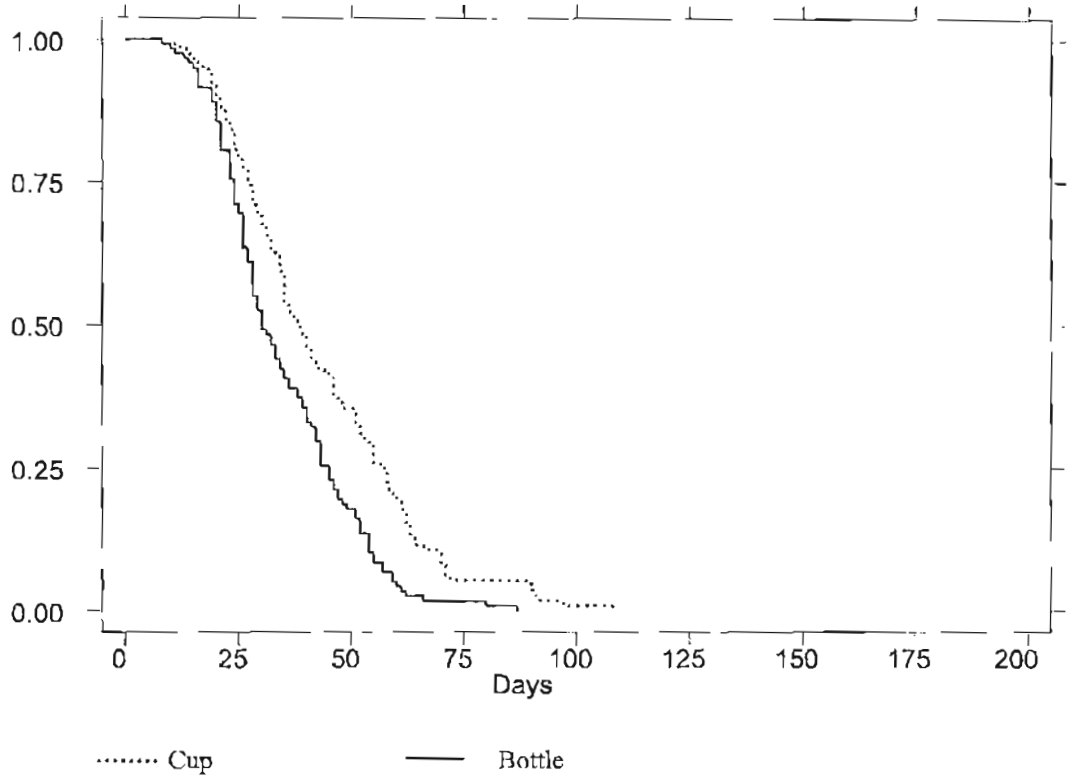


Table 6.20 Number of days to all sucking feeds, summary statistics: Cup versus Bottle, gestational age at birth greater than or equal to 28 weeks to less than 34 weeks

Days to all sucking feed	**Cup (n=118)**	**Bottle (n=119)**
	days (95% CI)	days (95% CI)
25th percentile	27 (24 to 31)	24 (21 to 26)
50th percentile	38 (34 to 45)	30 (28 to 35)
75th percentile	57 (51 to 62)	45 (40 to 51)

When an indicator for infants less than 28 weeks gestational age at birth was entered into the model this explained some but not all of the effect of cup feeding. Infants less than 28 weeks gestation at birth were six times more likely to take longer to reach all sucking feeds which was highly statistically significant (HR 6.06, 95% CI 4.16 to 8.80, P<0.001).

Gestational age at birth met the criteria for a 10% change in the hazard ratio, adjusting for this variable increases the hazard ratio from 1.50 to 1.75. The adjusted hazard ratio was retained (HR 1.75, 95% CI 1.34 to 2.28, P<0.001).

Figure 6.10 shows the Kaplan-Meier survival curves adjusted for gestational age at birth less than 28 weeks. In Table 6.21 the summary statistics are presented. When adjusting

for gestational age at birth less than 28 weeks, there is now a nine day increase in length of time to reach all sucking feeds for those randomised to cup feeds.

Figure 6.10 Kaplan-Meier survival estimates days to all sucking feeds, by cup or bottle allocation, adjusted for gestational age at birth less than 28 weeks.

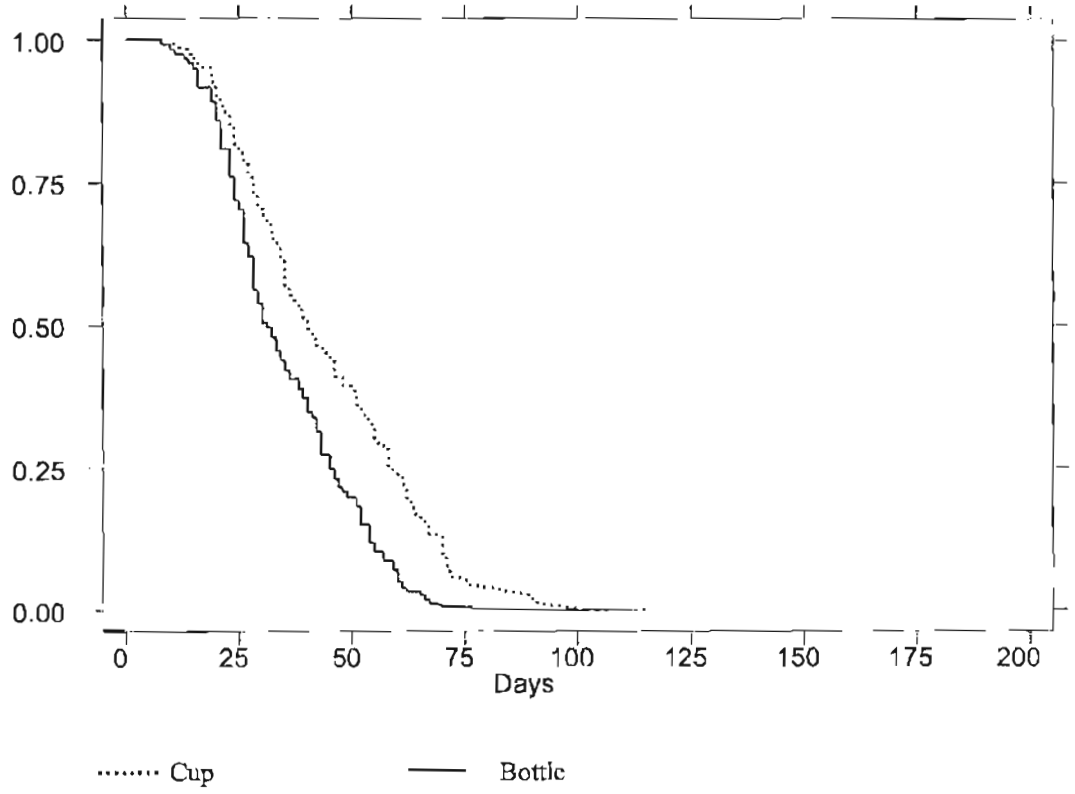


Table 6.21 Number of days to all sucking feeds, summary statistics: Cup versus Bottle, adjusted for gestational age at birth less than 28 weeks

Days to all sucking feed	Cup (n=118)	Bottle (n=119)
	days	days
25th percentile	27	23
50th percentile	40	31
75th percentile	58	45

6.4.6 Days to all sucking feeds by recruiting hospital and Cup versus Bottle

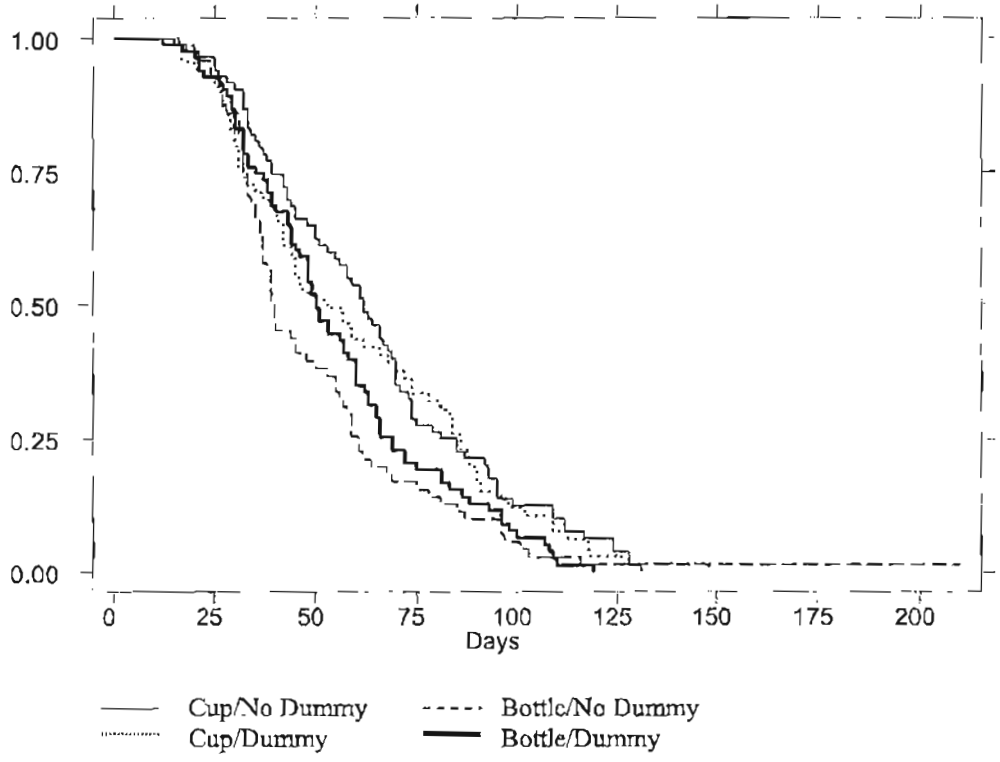
The effect of cup use on the outcome 'days to full sucking feeds' did not differ significantly between the two recruiting hospitals (test for interaction effect: HR 1.34, 95% CI 0.80 to 2.23, P=0.2). See Appendix XI: Outcomes by recruiting hospital for more detail.

6.5 *Duration of hospitalisation*

The duration of hospitalisation was calculated as the number of days from birth to discharge home, this included the number of days at WCH/MHW plus the number of days at the peripheral hospital. Cox proportional hazard models were used to estimate hazard ratios for the interventions. The dependence due to inclusion of twins was accounted for by using robust variance estimates, clustering on the mother. Infants who were withdrawn and those who died were included in the survival analysis, censoring at the time of last available data (n=16). The final discharge date was missing on two infants, censoring therefore occurred at time of transfer from WCH/MHW. 319 infants were therefore included in the survival analysis with censoring for 18 infants.

Figure 6.11 depicts the Kaplan-Meier survival curves for the four randomised groups. The Cup/No Dummy group had the longest length of hospital stay and Bottle/No Dummy the shortest.

Figure 6.11 Kaplan-Meier survival estimates duration of hospitalisation by randomised group



The summary statistics for each group are presented in Table 6.22.

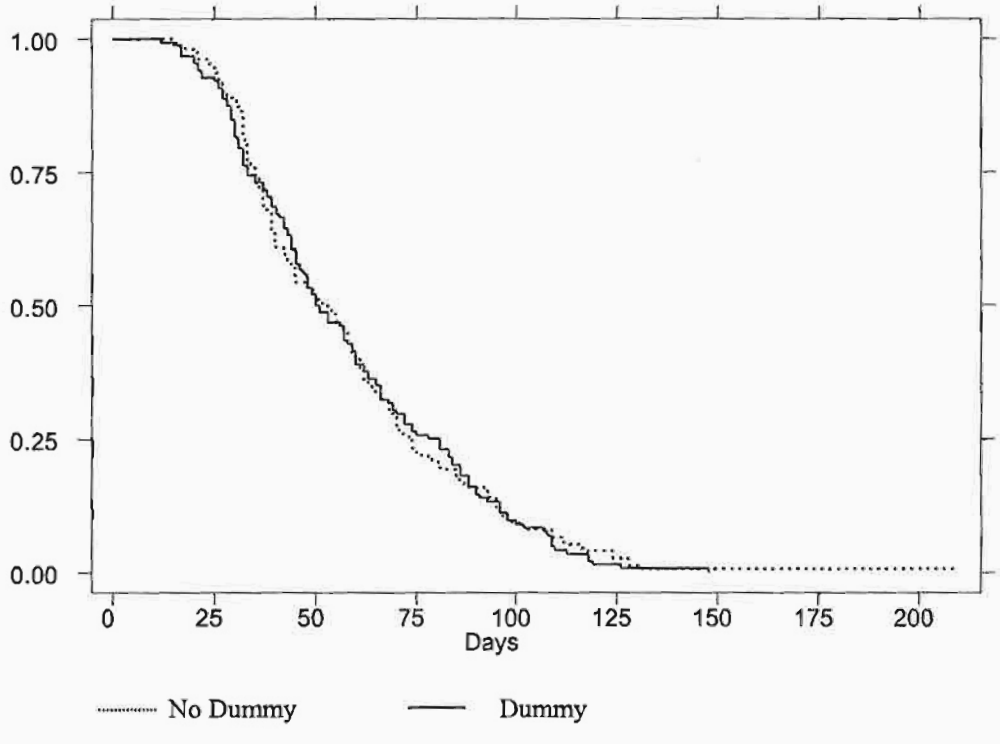
Table 6.22 Duration of hospitalisation, summary statistics by group randomised

Duration of hospitalisation	Cup/ No Dummy (n=89)	Cup/ Dummy (n=72)	Bottle/ No Dummy (n=73)	Bottle/ Dummy (n=85)	All groups (n=319)
	days	days	days	days	days
Median	62	53	40	50	51
Interquartile range	39-81	32-86	32-61	35-69	35-74

6.5.1 No Dummy versus Dummy

The Kaplan-Meier survival curves for the duration of hospitalisation according to No Dummy versus Dummy allocation are shown in Figure 6.12.

Figure 6.12 Kaplan-Meier survival estimates duration of hospitalisation by Dummy group



There was no significant difference in the length of stay between those randomised to No Dummy or those randomised to Dummy (HR 0.98, 95% CI 0.76 to 1.26, P=0.87). The summary statistics for No Dummy versus Dummy allocation are presented in Table 6.23.

Table 6.23 Duration of hospitalisation, summary statistics by dummy group

Duration of hospitalisation	No Dummy (n=162)	Dummy (n=157)
	Days (95% CI)	Days (95% CI)
25th percentile	35 (32-38)	33 (30-40)
50th percentile	53 (44-59)	51 (45-59)
75th percentile	74 (67-85)	78 (66-86)

6.5.2 Confounding – No dummy versus Dummy

Adjusting for potential confounding (parity, previous breast feeding experience and gestational age at birth) made minimal change to the hazard ratio and the unadjusted hazard ratio was retained (HR 0.98, 95% CI 0.76 to 1.26, P=0.87).

6.5.3 Cup versus Bottle

When analysed by Cup (n=161) versus Bottle (n=158) (Figure 6.13) the risk of a longer hospital stay was increased in those randomised to receive cup feeds (HR 1.41, 95% CI 1.09 to 1.82, P=0.01). Summary statistics are presented in Table 6.24. Those randomised to receive cup feeds had a median length of stay 11 days longer than those randomised to bottle feeds.

Figure 6.13 Kaplan-Meier survival estimates duration of hospitalisation, Cup versus Bottle

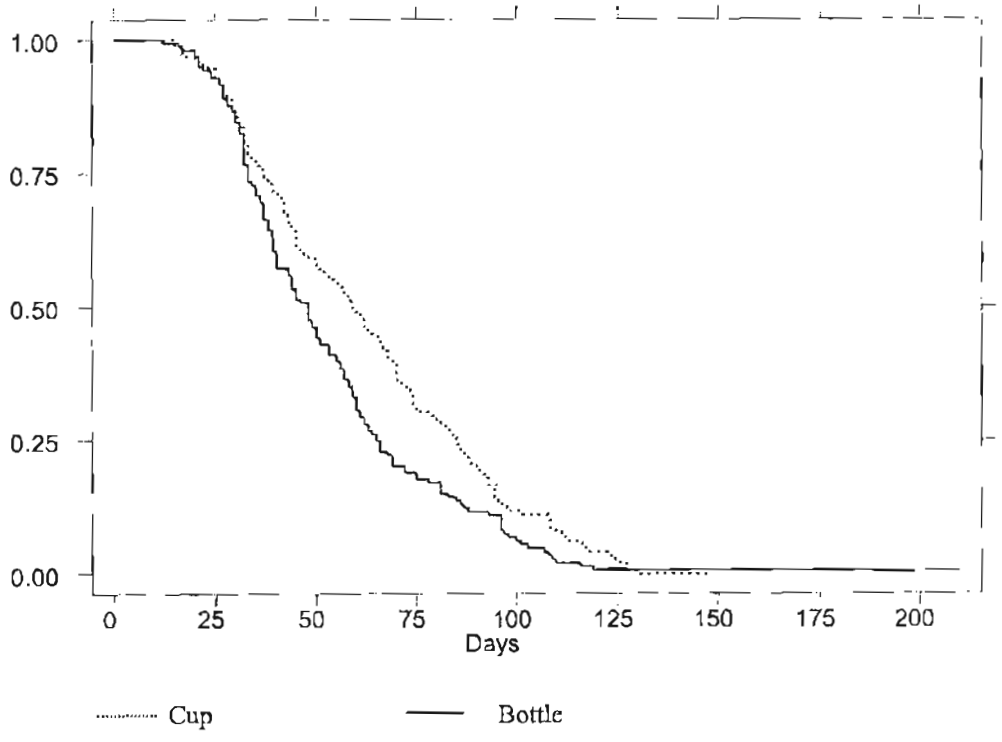


Table 6.24 Duration of hospitalisation, summary statistics Cup versus Bottle

Duration of hospitalisation	**Cup (n=161)**	**Bottle (n=158)**
	days (95% CI)	days (95% CI)
25th percentile	37 (32 to 42)	33 (32 to 37)
50th percentile	59 (50 to 67)	48 (40 to 53)
75th percentile	85 (74 to 92)	65 (60 to 75)

6.5.4 Confounding – Cup versus Bottle

Potential confounding variables, when analysed by Cup versus Bottle, included parity and gestational age at birth. Parity did not change the hazard ratio and was excluded from the model.

Infants who are more premature at birth take longer to mature, therefore require a longer duration of hospitalisation. There were a similar proportion of infants allocated to Cup and Bottle groups with gestational age at birth less than 28 weeks (Cup n=42, 26%; Bottle n=34, 22%). Figure 6.14 shows the Kaplan-Meier survival curves for the duration of hospitalisation for infants with gestational age at birth less than 28 weeks. The summary statistics are presented in Table 6.25, although the median length of stay was 93 days for those randomised to cup feeds and those to bottle feeds, the overall risk was for a longer length of stay for those randomised to cup feeds. The risk of a longer hospital stay remained significantly increased in those randomised to receive cup feeds and who were less than 28 weeks gestational age at birth (HR 1.81, 95% CI 1.06 to 3.09, P=0.03).

Figure 6.14 Kaplan-Meier survival estimates duration of hospitalisation, by Cup of Bottle allocation, for gestational age at birth less than 28 weeks.

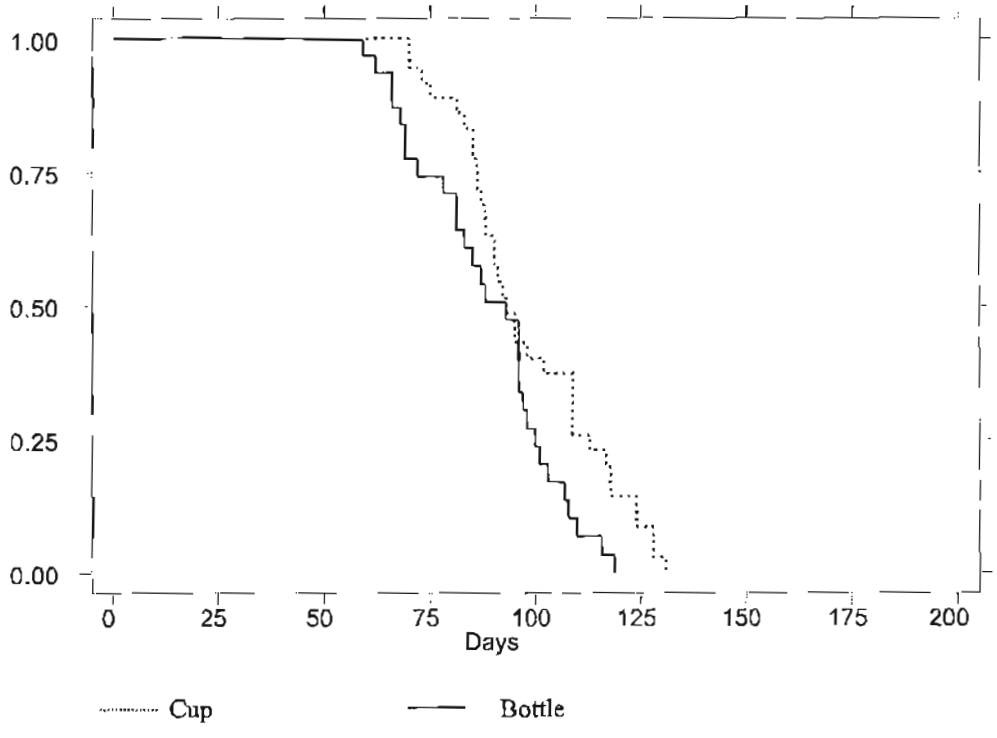


Table 6.25 Duration of hospitalisation, summary statistics Cup versus Bottle, gestational age at birth less than 28 weeks

Duration of hospitalisation	Cup (n=42)	Bottle (n=34)
	days (95% CI)	days (95% CI)
25th percentile	86 (75 to 90)	72 (66 to 85)
50th percentile	93 (88 to 109)	93 (81 to 97)
75th percentile	113 (98 to 124)	100 (96 to 108)

Figure 6.15 shows the Kaplan-Meier survival curves for the duration of hospitalisation for infants with gestational age at birth 28 to 34 weeks. The summary statistics are presented in Table 6.26. There was a five day difference in the median length of stay with those randomised to cup feeds hospitalised longer. The risk of a longer hospital stay remained significantly increased in those randomised to receive cup feeds and who were 28 to less than 34 weeks gestational age at birth (HR 1.44, 95% CI 1.08 to 1.92, P=0.01).

Figure 6.15 Kaplan-Meier survival estimates duration of hospitalisation, by Cup of Bottle allocation, for gestational age at birth 28 to less than 34 weeks.

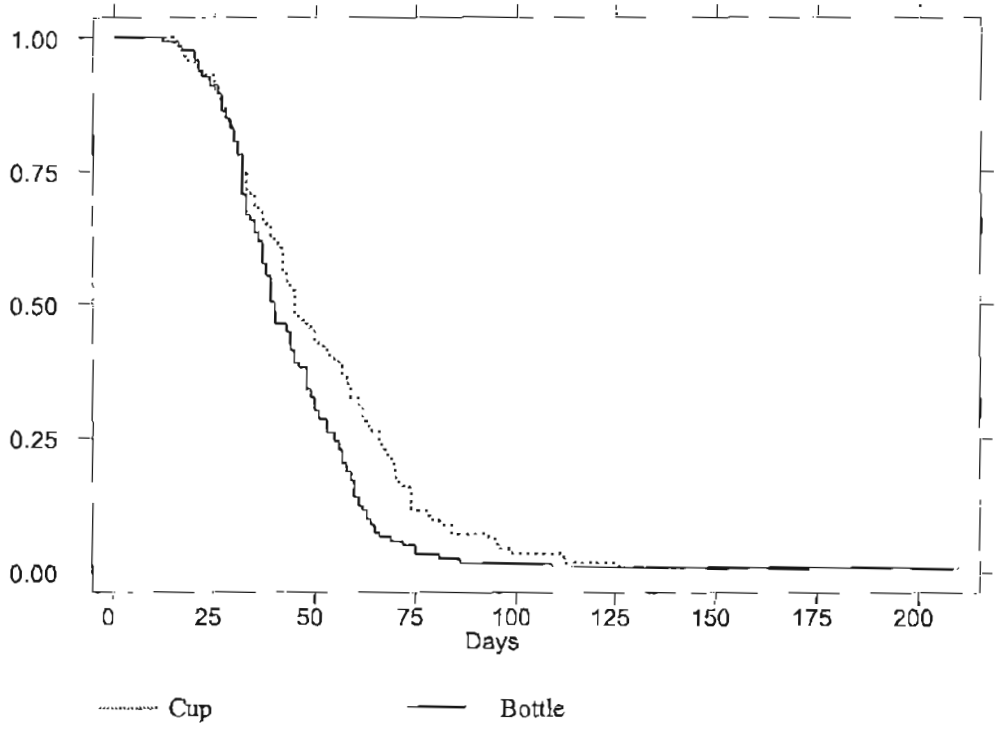


Table 6.26 Duration of hospitalisation, summary statistics Cup versus Bottle, gestational age at birth 28 to less than 34 weeks

Duration of hospitalisation	Cup (n=119)	Bottle (n=124)
	days (95% CI)	days (95% CI)
25th percentile	32 (30 to 37)	32 (30 to 33)
50th percentile	45 (42 to 53)	40 (37 to 44)
75th percentile	66 (59 to 71)	55 (49 to 59)

When infants less than 28 weeks gestational age at birth were entered into the model this explained some but not all of the effect of cup feeding. Gestational age at birth accounted for a 5% increase in the hazard ratio from 1.41 to 1.48 (95% CI 1.08 to 2.01, P=0.01).

None of the potential confounding variables met the initial criteria for a 10% change and the unadjusted hazard ratio was retained: HR 1.41, 95% CI 1.09 to 1.82, P=0.01.

6.5.5 Length of stay by recruiting hospital and Cup versus Bottle

The effect of cup use on length of hospital stay did not differ significantly between the two recruiting hospitals (test for interaction effect: HR 1.09, 95% CI 0.67 to 1.79, P=0.73). See Appendix XI: Outcomes by recruiting hospital for more detail.

6.6 *Weight gain*

Weight gain was calculated in grams per kilogram per day as follows:

Grams per kilogram per day = grams per day/average weight

where *Grams per day = (discharge weight – birth weight)/length of stay*

and *Average weight = (birth weight + discharge weight)/2*

The summary statistics for the four groups are presented in Table 6.27

Table 6.27 Weight gain, summary statistics by group randomised

Weight gain (g/kg/day)	Cup/ No Dummy (n=79)	Cup/ Dummy (n=66)	Bottle/ No Dummy (n=67)	Bottle/ Dummy (n=81)	All groups (n=293)
Mean ± SD	10.47 ± 2.35	9.99 ± 3.07	10.33 ± 3.29	10.34 ± 3.19	10.29 ± 2.97
Range	3.03 to 14.50	3.56 to 24.04	1.05 to 20.51	-3.29 to 16.01	-3.29 to 24.04

There was no significant difference in the weight gain between those randomised to No Dummy or those randomised to Dummy (t = -0.65, df 291, P=0.52, difference in means –0.23g/kg/day, 95% CI –0.91 to 0.46 g/kg/day). The summary statistics for No Dummy versus Dummy allocation are presented in Table 6.28.

Table 6.28 Weight gain, summary statistics No Dummy versus Dummy

Weight gain (g/kg/day)	No Dummy (n=146)	Dummy (n=147)
Mean ± SD	10.41 ± 2.81	10.18 ± 3.13
Range	1.05 to 20.51	-3.29 to 24.04

There was no significant difference in the weight gain between those randomised to Cup or those randomised to Bottle (t = 0.25, df 291, P=0.81, difference in means 0.09 g/kg/day, 95% CI –0.60 to 0.77 g/kg/day). The summary statistics for Cup versus Bottle allocation are presented in Table 6.29.

Table 6.29 Weight gain, summary statistics Cup versus Bottle

Weight gain (g/kg/day)	Cup (n=145)	Bottle (n=148)
Mean ± SD	10.25 ± 2.70	10.34 ± 3.23
Range	3.03 to 24.04	-3.29 to 20.51

The weight gain found in the study is lower than the expected weight gain for preterm infants of 15 grams/kg/day. Preterm infants lose approximately 10% - 20% of their birth weight after birth and can take approximately ten to twenty days to get back to their birth weight. The weight gain of 15 grams/kg/day is expected after infants have regained their birth weight. In this study only birth weight and discharge weights were recorded and so weight gain from time of regaining birth weight could not be calculated.

6.7 Feelings about participation in the trial

Mothers were asked at the six month post discharge questionnaire whether, if they were in the same situation, they would participate in such a study again. Possible responses were Yes, No and Maybe. Of the 252 questionnaires completed at the six month post discharge questionnaire, 220 responses were given to this question. Table 6.30 details the responses.

Table 6.30 Participate again

Participate again (total number respondents)	Cup & No Dummy (n=73)	Cup & Dummy (n=61)	Bottle & No Dummy (n=55)	Bottle & Dummy (n=63)	All groups Combined (n=252)
(n=66/53/48/53/220)	n (%)	n (%)	n (%)	n (%)	n (%)
Yes	51 (77)	40 (76)	43 (90)	49 (93)	183 (83)
No	0	1 (2)	1 (2)	4 (8)	2 (1)
Maybe	15 (23)	12 (23)	4 (8)	0	35 (16)

The majority of respondents would participate in such a study again. More in the Cup groups were unsure if they would participate again with approximately 20% answering 'Maybe' to this question.

Space was available for additional comments, 47 respondents (21%) took this opportunity. Comments were grouped into related themes and a content analysis of the themes was undertaken. The themes included research, feeding method and study design/management. Participant quotes are included as an example of the range of responses.

- *Research*

The comments were on the whole positive, 47% (n=22) of respondents commented on the importance of research and their willingness to take the opportunity to help those in the future who may have preterm infants. This included five who commented on the importance of this study in particular. Three answered that their participation would be dependent on the research. There were two negative comments, one stating it was time consuming, and one commented:

> *"I said yes to all the research and realised that was a problem later. I was bamboozled at the time after they were born."*

- *Feeding method*

There were five positive comments about the use of cup feeds as these quotes show:

> *"Because I found using a cup rather than a bottle when my baby was learning to feed was simple and not confusing to baby"*

> *"The study has helped me realise the importance of no bottles and dummies in the success of breast feeding"*

One commented: *"cup feeding is impossible if baby is upset"*

There were three positive comments about bottles:

> *"I would demand to put my baby on a bottle. I would not agree to have her on a cup"*

> *"We were in the control group which made it easier. I don't know that we would have stayed in the study if we had been in the cup groups as my baby really needed her bottle feeds"*

> *"... both of us can participate in his feed time"*

Two respondents made comments on the use of dummies.

> *"Would only do it if were in dummy group, as I feel premmies need the comfort of a dummy when they spend so much time on their own in an isolette."*

> *"Were times at home when I wished he'd taken a dummy but he wouldn't but I don't regret him not having one as I would only have been faced with removing it from him at some stage."*

- *Study management/design*

Five respondents commented on the management of the study or the study design as follows.

One comment was made against the study design:

> *"At times I found it hard to stick by the 'rules' of my particular combination of *BCD. I'd rather just do what was best for my baby instead of trying to continue adhering to the trial combinations"*
> *(BCD was the acronym for the trial – Bottles, cups and dummies)

One respondent commented on the support of staff for the trial:

> *"My baby was on cup feeds and the staff (except for a few) were not supportive of the cup. They gavaged my baby rather than cup fed – this was very distressing to us."*

Three respondents commented on the need for support for staff at the peripheral hospitals in their involvement in the trial, as this quote illustrates:

> *"The staff would have to be inserviced on how to cup feed as would both parents – also more information about the survey to the home hospital so staff are aware of it."*

Overall the majority of respondents would participate in such a study again but more respondents in the cup groups were unsure. Of those who made comments the majority were positive about the need for research in this population and their involvement. Some respondents highlighted the need for better support of staff and peripheral hospitals.

6.8 Summary of secondary study end points

The proportion of infants still receiving breast feeds at three and six months post discharge did not differ significantly between those randomised to 'no dummy' and those randomised to receive a dummy. There was a non significant trend for those randomised to cup feeds to have a higher breast feeding prevalence at three and six months post discharge. The most frequently cited reason for stopping breast feeding by three months post discharge was perceived insufficient milk supply. Dummy use had no effect on the number of days taken to reach all sucking feeds or length of hospitalisation. Those randomised to cup feeds had a significantly increased risk of a longer time to reach all sucking feeds and of hospitalisation. Those randomised to use of a dummy or cup showed no significant effect on weight gain. The majority of participants, if in the same situation, would participate in research for preterm infants.

Chapter 7. Exploratory sub-analyses

7.1 Introduction

Sub-analyses were performed to further explore the effects of not using a dummy and cup feeding on varying breast feeding outcomes. It is acknowledged that recombinations of the endpoints associated with these exploratory sub-analyses can lead to an increase in Type 1 error and caution is required in interpreting the results.

Twelve exploratory analyses were performed. Using the Bonferroni method to control for the inflation in Type 1 error consequent on multiple post hoc tests, significance is claimed when the test yields a P value less than 0.05 divided by the number of tests. Significance is therefore set at P=0.004 for these exploratory analyses.

7.2 Full/Nearly full breast feeding on discharge home

Labbok and Krasovec's revised breast feeding schema (Coffin et al. 1997) now includes a sub category of 'Full/Nearly full breast feeding' which comprises fully and high partial breast feeding. There was a higher proportion of infants in the No Dummy group with a high partial (>80%) breast feeding rate, that is over 8 out of the last 10 feeds prior to discharge home were breast feeds (either direct breast feeds or expressed breast milk) (Table 7.1). There was also a higher proportion in infants randomised to Bottle feeds with a high partial (>80%) breast feeding rate (Table 7.2).

Table 7.1 Breast feeding amounts on discharge home No Dummy versus Dummy

Breast feeding amounts	No Dummy groups (n=152)	Dummy groups (n=151)	All groups combined (n=303)
Fully	79 (52)	85 (56)	164 (54)
High partial (>80%)	14 (9)	6 (4)	20 (7)
Medium partial (20% - 80%)	9 (6)	15 (9)	24 (8)
Low partial (<20%)	1 (1)	1 (1)	2 (1)
Token	4 (3)	1 (1)	5 (2)
Nil	45 (30)	43 (29)	88 (29)

Table 7.2 Breast feeding amounts on discharge home Cup versus Bottle

Breast feeding amounts	Cup groups (n=151)	Bottle groups (n=152)	All groups combined (n=303)
Fully	92 (61)	72 (47)	164 (54)
High partial (>80%)	7 (5)	13 (9)	20 (7)
Medium partial (20% - 80%)	10 (7)	14 (9)	24 (8)
Low partial (<20%)	1 (1)	1 (1)	2 (1)
Token	2 (1)	3 (2)	5 (2)
Nil	39 (26)	49 (32)	88 (29)

To determine if there was an interaction effect between cup use and not using a dummy with the outcome 'Fully and High partial' breast feeding', a logistic regression was performed. The independent variables were the Cup groups (irrespective of dummy use) and No Dummy groups (irrespective of cup or bottle) with a multiplicative interaction term for Cup and No Dummy. The interaction was neither important nor statistically significant: OR 0.83, 95% CI 0.29 to 2.37, P=0.73. Comparisons can therefore be performed on the marginal groups No Dummy versus Dummy and Cup versus Bottle.

7.2.1 No Dummy versus Dummy

If the infants receiving greater than 80% breast feeds on discharge home are combined with the numbers fully breast feeding, there remains no significant difference between those randomised to No Dummy and those randomised to Dummy (Table 7.3).

Table 7.3 Summary results No Dummy versus Dummy 'Full/Nearly full breast feeding'

Fully & high partial breast feeding	No Dummy (n=152)	Dummy (n=151)		
	n (%)	n (%)	OR (95% CI)	P Value
Fully & high partial	93 (61)	91 (60)	1.04 (0.62 to 1.74)	0.88
***The rest**	59 (39)	60 (40)		

*(Medium & low partial, token and not breast feeding)

The effect of confounding was explored as described in Chapter 5 (section 5.2.6). Indicator variables were entered into the model where there was a 10% or greater difference in the distribution between the No Dummy and Dummy (parity, previous breast feeding experience) groups or where the indicator was identified a priori as a known predictor for breast feeding success (education, previous breast feeding experience and gestational age at birth). None of the indicator variables met the criteria for a 10% change in the odds ratio and the unadjusted odds ratio was retained.

No statistically significant difference was found between those randomised to No Dummy and Dummy for the outcome full/nearly full breast feeding on discharge home.

7.2.2 Cup versus Bottle

If the infants receiving greater than 80% breast feeds on discharge home are combined with the those fully breast feeding, they were 50% more likely to be 'fully and high partial' breast feeding on discharge home if they were randomised to cup feeds, this did not now reach statistical significance (Table 7.4).

Table 7.4 Summary results Cup versus Bottle 'Full/Nearly full breast feeding'

Fully & high partial breast feeding	Cup groups (n=151)	Bottle Groups (n=152)		
	n (%)	n (%)	OR (95% CI)	P Value
Fully & high partial	99 (66)	85 (56)	1.50 (0.89 to 2.53)	0.13
*The rest	52 (34)	67 (44)		

*(Medium partial, partial, token and not breast feeding)

The inclusion of 'high partial' breast feeding did not form part of the initial study hypothesis, and the alternate sub-categorisation of 'Full/Nearly Full breast feeding' (Coffin et al. 1997) had not been published when this study was designed. The study was powered to detect a 16.5% increase in the proportion of infants fully breast feeding compared to partial and not breast feeding from 45% to 61.5%. The pre-trial proportion for a combined group of 'high partial' and fully breast feeding cannot be determined as the baseline data were not collected in this format. A total sample size of 786 (cup 393 and bottle 393) would be required to detect a difference in the prevalence of breast feeding from 56% to 66%.

The effect of confounding was explored. There was a 10% or greater difference in the distribution between Cup and Bottle groups for parity; previous breast feeding experience, education and gestational age are known predictors for breast feeding success in preterm infants.

Gestational age at birth met the criteria for a 10% change in the odds ratio, increasing the odds ratio by 11% from 1.50 to 1.66, and the adjusted odds ratio was retained (adjusted OR 1.66, 95% CI 0.97 to 2.83, P=0.07). Infants randomised to cup feeds were more likely to be discharged home 'fully and high partial breast feeding' but this was not statistically significant.

7.3 *Fully breast feeding versus Not breast feeding on discharge home*

The study sample size was calculated to detect a difference in the numbers fully breast feeding compared to those partially and not breast feeding. Clinical and anecdotal experience at the time the study was designed suggested that mothers who were discharged home partially breast feeding were likely to stop breast feeding once home.

It is difficult to discern from the literature on trials reporting outcomes of breast feeding what comparison is being made when authors refer to exclusive or fully breast feeding. They do not state if they are comparing fully or exclusive to a combined group of partially and not breast feeding or only to those not breast feeding (Schubiger et al. 1997; Kliethermes et al. 1999; Kramer et al. 2001a; Kramer et al. 2001b). Gunn (2000) does not define the comparison but it can be determined from the graphical representation that exclusive breast feeding has been compared to the combined group of partial and not breast feeding (pp. 1360-1).

In comparing those fully breast feeding to a combined group of partially and not, the importance of those partially breast feeding is discounted. It may have been more correct to compare the proportion of those fully breast feeding with the proportion not breast feeding.

To determine if there was an interaction effect between cup use and not using a dummy a logistic regression was performed with fully breast feeding versus not breast feeding as the outcome variable. The interaction was neither important nor significant: OR 0.99, 95% CI 0.31 to 3.15, P=0.98. Comparisons can therefore be performed on the marginal groups No Dummy versus Dummy and Cup versus Bottle.

7.3.1 No Dummy versus Dummy

Infants were less likely to be fully breast fed compared to not breast fed if randomised to No Dummy; this was not statistically significant (Table 7.5)

Table 7.5 Summary results No Dummy versus Dummy – fully breast feeding versus not

	No Dummy (n=124)	**Dummy (n=128)**		
	n (%)	**n (%)**	**OR (95% CI)**	**P Value**
Fully breast feeding	79 (64)	85 (66)	0.89 (0.50 to 1.58)	0.69
Not breast feeding	45 (36)	43 (34)		

When adjusting for potential confounding (parity, previous breast feeding experience, education and gestational age at birth), education met the criteria for a 10% change to the unadjusted odds ratio, decreasing the odds ratio by 18% from 0.89 to 0.73. The adjusted odds ratio was therefore retained (adjusted OR 0.73, 95% CI 0.39 to 1.38, P=0.33).

No statistically significant difference was found between those randomised to No Dummy or Dummy on the outcome fully breast feeding versus not breast feeding on discharge home.

7.3.2 Cup versus Bottle

Infants were 61% more likely to be fully breast fed compared to not breast fed, however this did not reach statistical significance (Table 7.6)

Table 7.6 Summary results Cup versus Bottle – fully breast feeding versus not

	Cup groups (n=131)	Bottle Groups (n=121)		
	n (%)	n (%)	OR (95% CI)	P Value
Fully breast feeding	92 (70)	72 (60)	1.61 (0.90 to 2.87)	0.11
Not breast feeding	39 (30)	49 (41)		

When exploring the effect of confounding, education caused an 18% decrease in the odds ratio from 1.61 to 1.32, and gestational age at birth less than 28 weeks caused a 9% increase in the odds ratio from 1.61 to 1.75. Adjusting for these two variables accounted for an 11% decrease in the odds ratio from 1.61 to 1.44, the adjusted model was therefore retained (adjusted OR 1.44, 95% CI 0.76 to 2.74, P=0.27).

No statistically significant difference was found between those randomised to Cup feeds and those randomised to Bottle on the outcome fully breast feeding versus not breast feeding on discharge home.

7.4 Compliance analysis

The value in undertaking a compliance analysis is questionable (Haynes and Dantes 1987). The rationale behind doing so is that only those who complied have received the new intervention so the comparison should be between them and those who did not have the intervention. In doing so, however, the value of randomisation in controlling for

confounding is lost, there may be considerable differences between those receiving the intervention and those who did not comply with the intervention (Elwood 1998). Generalisation is not possible from a compliance analysis as the results are provided for a specific subgroup of patients (Chene et al. 1998). Further, bias may be introduced when doing a compliance analysis as compliance may be related to the outcome independently of the treatment received (Young et al. 1991; Chene et al. 1998). However, due to the very high rate of non compliance in this study, further exploratory analyses seemed reasonable, but need to be interpreted with caution.

Compliance analysis was performed on those who followed the protocol; those who did not follow part or all of the protocol for the group to which they were randomised withdrawn from the analysis, 192 infants with 172 mothers were included in the analysis.

The breast feeding status on discharge home for those who complied with the study protocol is shown in Table 7.7. The breast feeding prevalence (any) is higher for those who complied with the study protocol (80%), compared to the intention to treat analysis where 71% were breast feeding (any) on discharge home. Those randomised to the cup groups and who complied with their study allocation were virtually all breast feeding on discharge home (96% in the cup/no dummy group and 100% in the cup/dummy group). In contrast, for those randomised to the bottle groups and who complied with their study allocation approximately one third had stopped breast feeding (25% in the bottle/no dummy group and 32% in the bottle/dummy group).

Table 7.7 Breast feeding status on discharge home for compliers.

Breast feeding status	**Cup/ No Dummy (n=28)**	**Cup/ Dummy (n=34)**	**Bottle/ No Dummy (n=48)**	**Bottle/ Dummy (n=82)**	**All groups Combined (n=192)**
	n (%)	n (%)	n (%)	n (%)	n (%)
Any breast feeding	27 (96)	34 (100)	36 (75)	56 (68)	153 (80)
Fully	*23 (82)*	*30 (88)*	*25 (52)*	*41 (50)*	*119 (78)*
Partially	*4 (14)*	*4(12)*	*11 (23)*	*15 (18)*	*34 (22)*
Not breast feeding	1 (4)	0 (0)	12 (24)	26 (32)	39 (20)

7.4.1 No Dummy versus Dummy

Among those who complied there were differences in the baseline demographic and clinical characteristics when analysed by No Dummy versus Dummy groups (Table 7.8 and Table 7.9). Those who complied with the study protocol and were in the No Dummy groups had a 10% or greater difference in the following variables: more women were

primiparous, had completed High School and their main source of household income was full time work, fewer had planned to breast feed for six months or less and, although a similar proportion in both groups had breast fed before, more in the No Dummy groups had breast fed for longer than six months. Fewer infants in the No Dummy groups required respiratory support (IPPV and CPAP).

Table 7.8 Maternal characteristics of those who complied with the study protocol.

Characteristic (Total number respondents)	Complied No Dummy groups (n=69 mothers)	Complied Dummy groups (n=103 mothers)
	n (%)	(n %)
*Maternal age (n=68/103)	30.4±5 (19-42)	28.7±6 (15-41)
Parity (n=69/103)		
Primiparous	28 (41)	58 (56)
Multiparous	41 (59)	45 (44)
Lives with another adult (n=68/97)	68 (100)	88 (91)
Education (n=66/97)		
Incomplete HS	12 (18)	37 (38)
Complete HS	25 (38)	27 (28)
Tertiary	29 (44)	33 (34)
Main income source (n=68/95)		
Part time work	5 (7)	1 (1)
Full time work	60 (88)	72 (76)
Benefits	3 (4)	22 (23)
During pregnancy planned to breast feed (68/98)		
Yes	65 (96)	95 (97)
No	3 (4)	3 (3)
Length of time planned to breast feed (65/95)		
≤6 weeks	1 (2)	3 (3)
>6 weeks to ≤3 months	0	5 (5)
>3 months to ≤6 months	12 (19)	19 (20)
>6 months	41 (63)	52 (55)
Don't know	11 (17)	16 (17)
Breast fed before (n=68/98)		
Yes	28 (41)	33 (34)
No	40 (59)	65 (66)
Length of time breast fed before (68/98)		
Never	40 (59)	65 (66)
≤6 weeks	5 (7)	8 (8)
>6 weeks to ≤3 months	1 (2)	6 (6)
>3 months to ≤6 months	5 (7)	8 (8)
>6 months	17 (25)	11 (11)

*Mean±SD (Range)

Table 7.9 Neonatal characteristics of those who complied with the study protocol.

Characteristic (Total number respondents)	Complied No Dummy groups (n=76 infants)	Complied Dummy groups (n=116 infants)
Hospital (n=76/116)		
WCH	17 (22)	38 (33)
MHW	59 (78)	78 (67)
Twins (n=76/116)		
Twins	15 (20)	26 (22)
Singleton	61 (80)	90 (78)
Method of delivery (n=76/115)		
Vaginal	27 (36)	36 (31)
Instrument	6 (8)	8 (7)
Caesarean	43 (57)	71 (62)
*Birth weight, grams (76/116)	1460±459 (500-2580)	1583±437 (614-2520)
Gestation at birth (n=76/116)		
<28 weeks	6 (8)	20 (17)
28 - <34 weeks	70 (92)	96 (83)
Respiratory support		
Oxygen use ≥ 1 day (n=76/115)	56 (74)	86 (75)
IPPV (n=76/116)	36 (47)	71 (61)
CPAP (n=76/116)	33 (43)	61 (53)
Home oxygen (n=62/130)	4 (5)	11 (10)
Separation (76/116)		
Discharged directly home	24 (32)	44 (38)
Transferred to peripheral hospital then discharged home	52 (68)	72 (62)

*Mean±SD (Range)

Table 7.10 shows the prevalence of breast feeding on discharge home according to randomisation to no dummy or dummy group for those who complied with the study protocol.

Table 7.10 Breast feeding prevalence No Dummy versus Dummy – compliers

Breast feeding status	No Dummy (n=76)	Dummy (n=116)
	n (%)	n (%)
Any breast feeding	63 (83)	90 (78)
Fully	*48 (63)*	*71 (61)*
Partially	*15 (20)*	*19 (17)*
Not breast feeding	13 (17)	26 (22)

7.4.1.1 Outcome fully breast feeding

Among those who complied with their allocated study protocol there was no statistically significant difference between those randomised to No Dummy versus Dummy groups for the outcome fully breast feeding (compared to partially and not) (OR 1.09, 95%CI 0.556 to 2.09, P=0.80). Indicator variables were entered in the model where there was a 10% or greater difference in distribution (recruiting hospital, parity, education, main income

source, length of time planned to breast feed, length of time breast fed before, required IPPV and CPAP) and for known predictors for breast feeding success (previous breast feeding experience and gestational age at birth).

The indicator variables education, main household income source, length of time breast fed before, previous breast feeding experience and gestational age each met the criteria for a 10% change in the odds ratio, and together decreased it by 45% from 1.09 to 0.60 and all were therefore retained (adjusted OR 0.60, 95% CI 0.26 to 1.37, P=0.22).

Those complying with the study allocation and randomised to No Dummy groups were less likely to be fully breast feeding on discharge home, but this was not statistically significant.

7.4.1.2 Outcome any breast feeding

Those who complied with the study protocol and were randomised to the No Dummy groups were more likely to be breast feeding (fully and partially combined) but this was not statistically significant (OR 1.40, 95% CI 0.63 to 3.12, P=0.41).

On adjusting for potential confounding, education, main source of household income, length of time breast fed before, previous breast feeding experience and gestational age at birth each caused a 10% or greater change in the odds ratio. When these variables were entered into the model the odds ratio decreased by 46% from 1.40 to 0.75 and the adjusted model was retained (adjusted OR 0.75, 95% CI 0.40 to 1.41, P=0.37).

Those who complied with the study protocol and were randomised to the No Dummy groups were more likely to be breast feeding (fully and partially combined) but this was not statistically significant.

7.4.1.3 Days to all sucking feeds and length of hospital stay

For those who complied with the study protocol and were randomised to No Dummy or Dummy there was no statistically significant difference in the time taken to reach full sucking feeds (HR 1.20, 95% CI 0.88 to 1.64, P=0.24) or in the length of hospital stay (HR 1.30, 95% CI 0.95 to 1.78, P=0.10). Summary statistics are presented in Table 7.11.

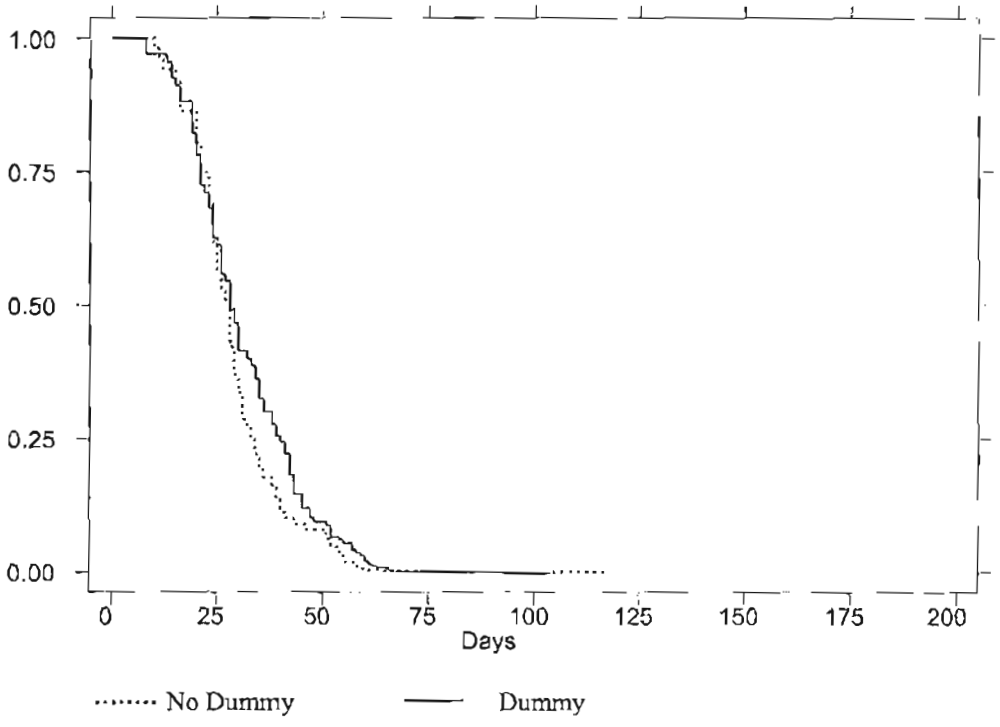
Table 7.11 Days to all sucking feeds and Duration of hospitalisation, summary statistics Cup versus Bottle

Percentile	No Dummy (n=76)	Dummy (n=116)
	days	days
*Days to all sucking feeds	31 (24-52)	39 (25-58)
*Length of hospitalisation	38 (32-61)	48 (32-66)

*Median (interquartile range)

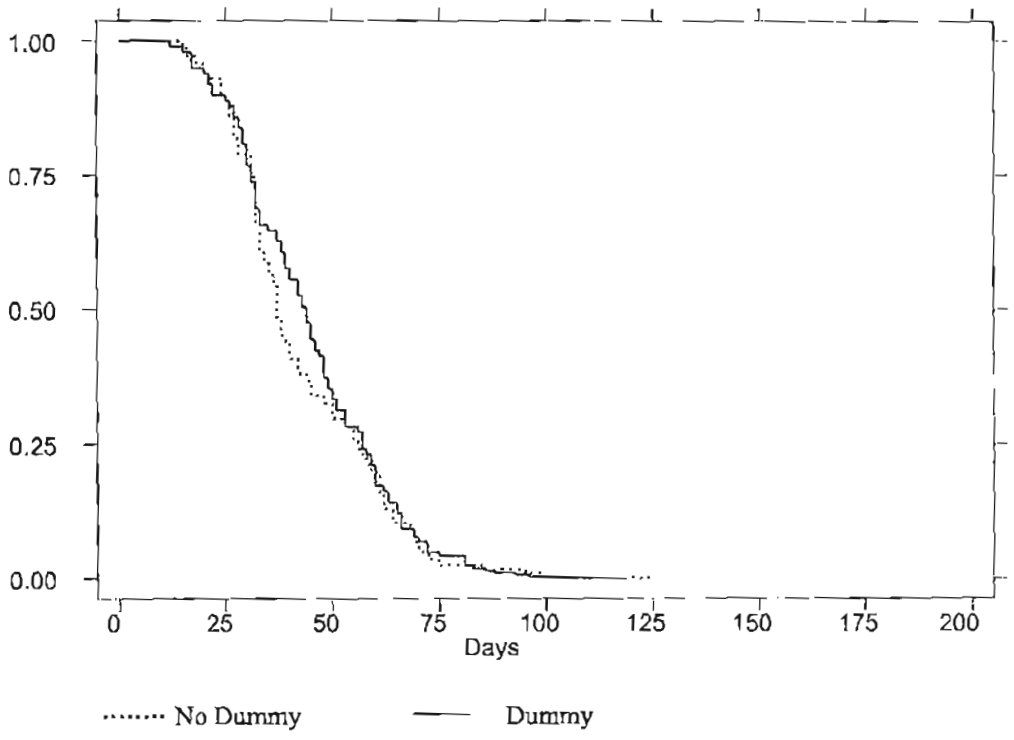
When adjusting for the effect of confounding for the outcome days to all sucking feeds, gestational age and requiring IPPV caused a 10% or greater change in the hazard ratio. Adjusting for these variables reduced the hazard ratio by 19% from 1.20 to 0.97 and the adjusted model was retained (adjusted HR 0.97, 95% CI 0.70 to 1.35, P=0.87) (Figure 7.1).

Figure 7.1 Kaplan-Meier survival estimates days to all sucking feeds, by No dummy or Dummy allocation, adjusted for gestational age at birth less than 28 weeks and IPPV.



Adjusting for the effect of confounding for the outcome length of hospital stay, gestational age caused a 17% reduction in the hazard ratio from 1.30 to 1.08 and therefore the adjusted model was retained (adjusted HR 1.08, 95% CI 0.77 to 1.51, P=0.67) (Figure 7.2).

Figure 7.2 Kaplan-Meier survival estimates length of hospital stay, by No dummy or Dummy allocation, adjusted for gestational age at birth less than 28 weeks.



7.4.2 Cup versus Bottle

Among those who complied there were differences in the baseline demographic and clinical characteristics between those randomised to the Cup and Bottle groups (Table 7.12 and Table 7.13). Those who complied with the study protocol and were in the Cup groups had fewer twins, more of the mothers were primiparous with a tertiary education, more had planned to breast feed for longer than six months and of those who had breast fed before, a greater proportion had breast fed for longer than six months.

Table 7.12 Maternal characteristics of those who complied with the study protocol.

Characteristic (Total number respondents)	Complied Cup groups (n=60 mothers)	Complied Bottle groups (n=112 mothers)
	n (%)	(n %)
*Maternal age (n=59/111)	29±6.2 (16-42)	29±5.6 (15-39)
Parity (n=60/112)		
Primiparous	37 (62)	49 (44)
Multiparous	23 (38)	63 (56)
Lives with another adult (n=60/105)	57 (95)	99 (95)
Education (n=60/103)		
Incomplete HS	14 (23)	35 (34)
Complete HS	18 30)	34 (33)
Tertiary	28 (47)	34 (33)
Main income source (n=60/103)		
Part time work	2 (3)	4 (4)
Full time work	49 (82)	83 (80)
Benefits	9 (15)	16 (16)
During pregnancy planned to breast feed (60/106)		
Yes	60 (100)	100 (94)
No	0	6 (6)
Length of time planned to breast feed (60/100)		
≤6 weeks	0	4 (4)
>6 weeks to ≤3 months	1 (2)	4 (4)
>3 months to ≤6 months	10 (17)	21 (21)
>6 months	39 (65)	54 (54)
Don't know	10 (17)	17 (17)
Breast fed before (n=60/106)		
Yes	20 (33)	41 (39)
No	40 (67)	65 (61)
Length of time breast fed before (60/106)		
Never	40 (67)	65 (61)
≤6 weeks	3 (5)	10 (9)
>6 weeks to ≤3 months	0	7 (7)
>3 months to ≤6 months	2 (3)	11 (10)
>6 months	15 (25)	13 (12)

*Mean±SD (Range)

Table 7.13 Neonatal characteristics of those who complied with the study protocol.

Characteristic (Total number respondents)	Complied Cup groups (n=62 infants)	Complied Bottle groups (n=130 infants)
Hospital (n=62/130)		
WCH	19 (31)	36 (28)
MHW	43 (69)	94 (72)
Twins (n=62/130)		
Twins	4 (7)	37(28)
Singleton	58 (94)	93 (72)
Method of delivery (n=62/129)		
Vaginal	21 (34)	42 (33)
Instrument	2 (3)	12 (9)
Caesarean	39 (63)	75 (58)
*Birth weight, grams	1557±467 (614-2560)	1494±457 (500-2580)
Gestation at birth (n=62/130)		
<28 weeks	5 (8)	21 (16)
28 - <34 weeks	57 (92)	109 (84)
Respiratory support		
Oxygen use ≥ 1 day (n=61/130)	45 (74)	97 (75)
IPPV (n=62/130)	32 (52)	75 (58)
CPAP (n=62/130)	27 (44)	67 (52)
Home oxygen (n=62/130)	5 (8)	10 (8)
Separation (62/130)		
Discharged directly home	24 (39)	44 (34)
Transferred to peripheral hospital then discharged home	38 (61)	86 (66)

*Mean±SD (Range)

Table 7.14 shows the prevalence of breast feeding on discharge home according to randomisation to cup or bottle for those who complied with the study protocol.

Table 7.14 Breast feeding prevalence Cup versus Bottle – compliers

Breast feeding status	Cup (n=62)	Bottle (n=130)
	n (%)	n (%)
Any breast feeding	61 (99)	92 (71)
Fully	*53 (86)*	*66 (51)*
Partially	*8 (13)*	*26 (20)*
Not breast feeding	1 (2)	38 (29)

7.4.2.1 Outcome fully breast feeding

Those who complied with the study protocol and were randomised to the Cup groups were significantly more likely to be fully breast feeding on discharge home (OR 5.71, 95% CI 2.54 to 12.84; P<0.001). Indicator variables were entered in the model where there was a 10% or greater difference in distribution (recruiting hospital, parity, education, length of time planned to breast feed, length of time breast fed before, twins) and for known

predictors for breast feeding success (previous breast feeding experience and gestational age at birth).

Education was the only indicator variable that met the criteria for a 10% change in the odds ratio, decreasing 11% from 5.71 to 5.10 and therefore was retained (adjusted OR 5.10, 95% CI 2.24 to 11.63, P<0.001).

Those complying with the study allocation and randomised to Cup feeds were five times more likely to be fully breast feeding on discharge home, which statistically significant at P=0.004 level.

7.4.2.2 Outcome any breast feeding

Those who complied with the study protocol and were in the Cup groups were significantly more likely to have any breast feeding on discharge home, however, the confidence intervals are extremely wide (OR 25.20, 95% CI 3.32 to 191.02; P=0.002).

On adjusting for confounding parity, education, length of time breast fed before and twins caused a 10% or greater change in the odds ratio. When these variables were entered into the model the odds ratio decreased by 16% from 25.20 to 21.09, the unadjusted model was therefore retained (adjusted OR 21.09, 95% CI 2.62 to 169.75, P=0.004), those who complied with the study protocol and were in the Cup groups were significantly more likely to have any breast feeding on discharge home.

7.4.2.3 Days to all sucking feeds and length of hospital stay

In contrast to the intention to treat analysis, with the compliance analysis there was no increase in risk of the cup groups taking longer to reach full sucking feeds (HR 1.18, 95% CI 0.86 to 1.61, P=0.30) or in having a longer length of hospital stay (HR 1.02, 95% CI 0.74 to 1.41, P=0.89). Summary statistics are presented in Table 7.15.

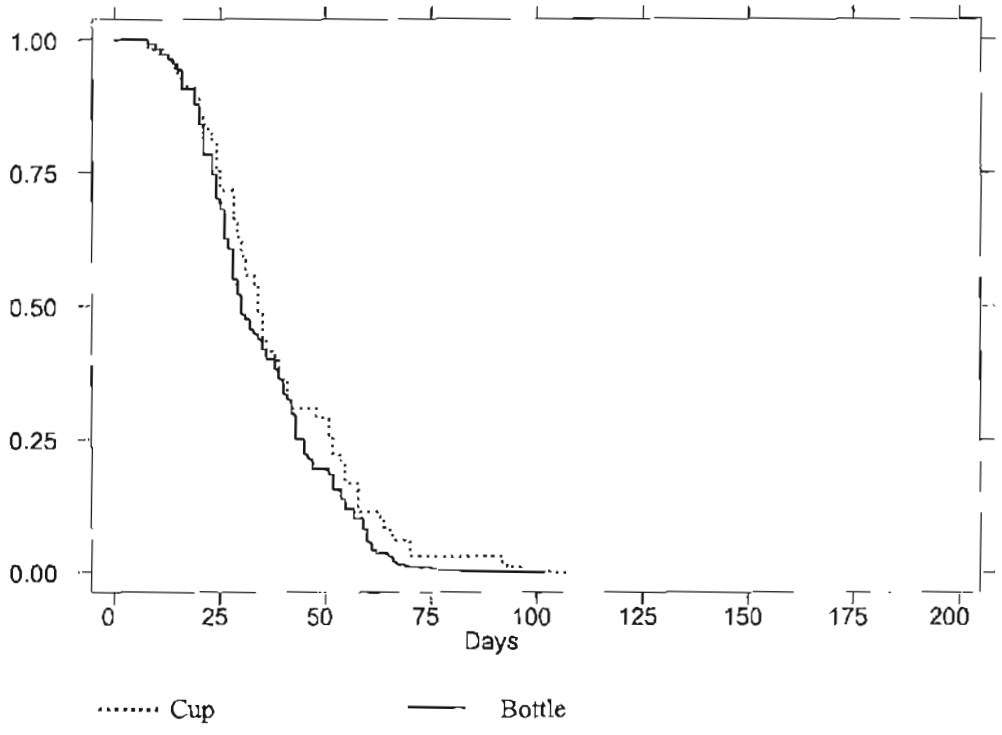
Table 7.15 Days to all sucking feeds and Duration of hospitalisation, summary statistics Cup versus Bottle

Percentile	Cup (n=62)	Bottle (n=130)
	days	days
*Days to all sucking feeds	35 (25, 55)	35 (24, 54)
*Length of hospitalisation	42 (31, 61)	45 (32, 63)

*Median (interquartile range)

When adjusting for the effect of confounding for the outcome days to all sucking feeds, gestational age at birth met the criteria for a 10% or greater change in the hazard ratio. Including this variable in the model increased the hazard ratio by 26% and the adjusted model was retained (adjusted HR 1.49, 95% CI 1.05 to 2.13, P=0.02) (Figure 7.3). Those randomised to cup and who complied with the protocol now had an increased risk for a longer time to reach all sucking feeds than those randomised to Bottle, which did not reach significance at the P=0.004 level.

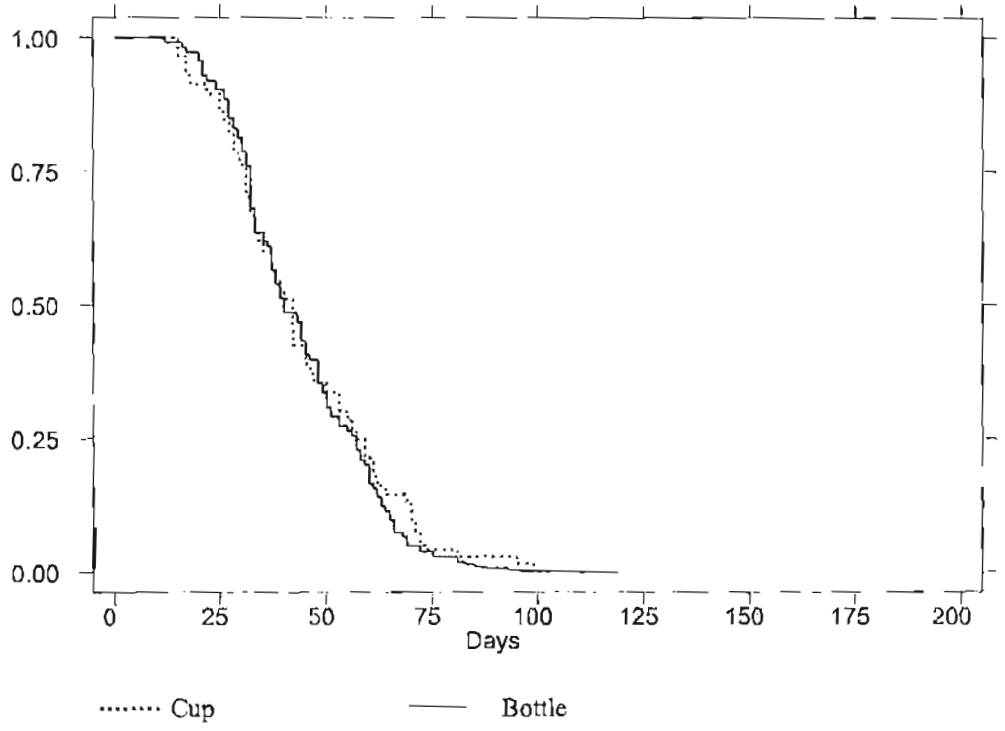
Figure 7.3 Kaplan-Meier survival estimates days to all sucking feeds, by cup or bottle allocation, adjusted for gestational age at birth less than 28 weeks.



When adjusting for the affect of confounding for the outcome length of hospital stay, gestational age at birth increased the hazard ratio by 20% and the adjusted model was retained (adjusted HR 1.22, 95%CI 0.86 to 1.727, P=0.27) (Figure 7.4). In contrast to the

intention to treat analysis those randomised to cup feeds and who complied with the protocol did not have a statistically significant difference in length of hospital stay.

Figure 7.4 Kaplan-Meier survival estimates length of hospital stay, by cup or bottle allocation, adjusted for gestational age at birth less than 28 weeks.



7.4.2.4 Summary compliance analysis

The purpose of compliance analyses as a complement to an intention to treat analyses, are to explore hypotheses for subsequent evaluation (Young et al. 1991; Chene et al. 1998).

Those complying with the study protocol and randomised to No Dummy groups showed no statistically significant difference in breast feeding outcomes, days to all sucking feeds or length of hospital stay which agrees with the intention-to-treat analysis. In contrast, those who complied with the study protocol and were randomised to Cup feeds compared to those who complied with the study protocol and were randomised to Bottle feeds, had quite differing outcomes to the intention-to-treat analysis. Breast feeding outcomes (fully and any) were significantly greater for those complying with Cup feeding, days to all sucking feeds remained significantly increased but there was no significant difference in length of stay.

Women who complied with the study protocol and were randomised to the Cup groups were more educated than those who complied with the study protocol and were randomised to the Bottle groups. In addition, fewer had infants less than 28 weeks gestation at birth, and, although a similar proportion of women in both groups had breast fed before, more in the Cup group had breast fed previously for longer than six months compared to those in the Bottle group. These variables have been shown to be predictive of breast feeding outcomes in the preterm population (Kaufman and Hall 1989; Boo and Goh 1999; Killersreiter et al. 2001; Furman et al. 2002). Women complying with the study protocol and randomised to the Cup groups had fewer twins than those complying with the study protocol and randomised to the Bottle groups. This contrasts with the work of others where twins have been associated with success in breast feeding (Killersreiter et al. 2001). More women who complied with the study protocol and were randomised to the Cup groups were primiparous. Parity has not been shown to be related either to continuing or stopping breast feeding in the preterm population. In contrast, in the term infant population multiparity has been reported to be associated with longer breast feeding duration (Vogel et al. 1999).

7.5 Summary of exploratory sub-analyses

Those randomised to cup feeds had a higher proportion of infants 'Full/Nearly full' breast feeding than those randomised to bottle feeds, which did not reach statistical significance. There was a higher proportion of infants fully breast feeding compared to not breast feeding in those randomised to cup feeds which also did not reach significance. On compliance analysis (adjusted for confounding), those who cup fed had an increased odds ratio of fully and any breast feeding. When adjusting for confounding those who cup fed had an increased risk of taking longer to reach all sucking feeds but no increase in risk for a longer hospital stay. The compliance analysis results need to be interpreted with caution and generalisations cannot be made, however it highlights the need for further research in regard to the effect of cup feeding on the outcomes any breast feeding on discharge home and length of hospital stay.

Chapter 8. Discussion of results from the randomised controlled trial

This is the third and largest randomised controlled trial to assess the effect cup feeding has on breast feeding outcomes in preterm infants. It is the first randomised controlled trial to assess the effect the use of dummies has on breast feeding outcomes in this population.

8.1 Key findings

8.1.1 Interaction between No Dummy and Cup

There was no interaction effect between using a dummy and using a cup. Therefore, preterm infants who were randomised to use a cup and not use a dummy did not have better breast feeding outcomes than preterm infants randomised to use a cup and a dummy. The effect dummies have on breast feeding outcomes could therefore be analysed independently of the effect of cup or bottle.

8.1.2 No Dummy versus Dummy

Breast feeding

Not using a dummy did not significantly affect the proportion of infants fully breast feeding on discharge home (OR 0.84, 95% CI 0.51 to 1.39, P=0.50), or 'any' breast feeding on discharge home (adjusted OR 0.83, 95% CI 0.45 to 1.50, P=0.53). Not using a dummy also made no significant difference to breast feeding prevalence at three or six months post discharge.

Time to full sucking feeds/Duration of hospitalisation

There was no increase in risk associated with not using a dummy on the time taken to reach full sucking feeds (HR 0.94, 95%CI 0.73 to 1.20, P=0.61), or on the length of hospital stay (HR 0.98, 95% CI 0.76 to 1.26, P=0.87).

8.1.2.1 Comparison with findings from other studies

Breast feeding

This is the first study to assess the effect of dummy use on breast feeding outcomes in the preterm infant population. Although comparison with term infants is not appropriate due to the difference in establishing sucking feeds for preterm infants, the only studies that have assessed the effect of dummies on breast feeding outcomes have been in the term infant population.

Several observational studies in term infants showed a significant relationship between dummy use and early weaning (Victora et al. 1993; Ford et al. 1994; Barros et al. 1995; Righard and Alade 1997; Victora et al. 1997; Aarts et al. 1999; Howard et al. 1999b; Vogel et al. 2001). A randomised controlled trial of counselling to avoid dummy use compared with counselling to include dummy use in the care of term infants reduced dummy use and had no impact on breast feeding prevalence at three months of age (Kramer et al. 2001a). The reduction in dummy use achieved in Kramer's (2001a) study was small, 61% in the experimental group still used a dummy compared with 84% in the control group. In the study reported in this thesis 31% randomised to No Dummy used a dummy compared to 99% of those randomised to receive a Dummy.

A more recent randomised controlled trial showed contrasting results (Howard et al. 2003). Infants randomised to early dummy (introduced at 2 - 5 days) compared to late dummy (to be introduced at 5 weeks) showed a significantly reduced prevalence of exclusive breast feeding at four weeks post partum (OR 1.5, 95% CI 1.0 to 2.0, P=0.03) but did not significantly affect full or any breast feeding. Early dummy introduction also significantly reduced the duration of any breast feeding (adjusted HR 1.20, 95% CI 1.02 to 1.42, P=0.03).

The study reported in this thesis provides no evidence to support not using a dummy in the preterm population as a strategy to increase breast feeding outcomes.

Time to full sucking feeds

Five randomised controlled trials have examined the effect of dummy use and non-nutritive sucking on transition time to full bottle feeds in preterm infants (Measel and Anderson 1979; Field et al. 1982; Bernbaum et al. 1983; Sehgal et al. 1990; Mattes et al. 1996). Both Measel et al. (1979) and Field et al. (1982) found that infants who used a

dummy during tube feeds had on average 27 fewer tube feedings than those who did not use a dummy. Bernbaum et al. (1983) showed a decrease in the number of days to reach full sucking feeds of six days (P<0.001) for infants who used a dummy during tube feeds and Sehgal et al. (1990) 1.6 days (P<0.001), Mattes et al. (1996) found no differences in time to reach full sucking feeds. These trials were small with numbers ranging from 30 to 59 infants, all of who were being artificially fed.

The study reported in this thesis is the largest randomised controlled trial to evaluate the effect of dummies on time to reach all sucking feeds. It therefore provides considerable weight to the conclusion of Mattes et al. (1996) that the use of dummies does not accelerate sucking maturation and therefore does not reduce the number of days to all sucking feeds.

Duration of hospitalisation

Duration of hospital stay was found to be reduced by four to eight days in the three trials in which this was measured (Measel and Anderson 1979; Field et al. 1982; Bernbaum et al. 1983). A meta-analysis was conducted on two of these studies (Field et al. 1982; Bernbaum et al. 1983) and showed a significant reduction in hospital stay (WMD -7.1 days, 95% CI -12.6 to -1.7) (Pinelli and Symington 2003). These trials were small with 30 to 59 infants participating, all of whom were being artificially fed.

The study reported in this thesis is the largest randomised controlled trial to evaluate the effect of dummies on duration of hospitalisation. It therefore provides strong evidence to suggest that the use of dummies does not reduce the length of hospital stay.

8.1.3 Cup versus Bottle

Breast feeding

Infants randomised to cup feeds were significantly more likely to be fully breast fed on discharge home (OR 1.73, 95%CI 1.04 to 2.88, P=0.03). Infants were more likely to have 'any' breast feeding if they had cup feeds, however this did not reach statistical significance (OR 1.37, 95% CI 0.78 to 2.38, P=0.27). The sample size in this study could have detected a 14.5% difference in the outcome any breast feeding, a sample size of 1,860 would be needed to test if the difference found in this study was a statistically significant difference.

When infants receiving greater than 80% breast feeds on discharge home were combined with the numbers fully breast feeding, those randomised to cup feeds were 66% more likely to be 'fully and high partial' breast feeding, however this did not reach significance (adjusted OR 1.66, 95% CI 0.97 to 2.83, P=0.07).

The inclusion of 'high partial' breast feeding did not form part of the initial study hypothesis, and the alternate sub-categorisation of 'Full/Nearly Full breast feeding' (Coffin et al. 1997) had not been published when this study was designed. The study was powered to detect a 16.5% increase in proportion of infants fully breast feeding on discharge home from 45% to 61.5%. The pre-trial rates for a combined group of 'high partial' and fully breast feeding cannot be determined as the baseline data were not collected in this format. The study may therefore have been under-powered to detect a difference when 'high partial' breast feeding was included. This exploratory analysis therefore needs to be interpreted with caution.

There was a trend for those randomised to cup feeds to have a higher rate of 'any' breast feeding at three and six months but this did not reach statistical significance.

Time to full sucking feeds/Duration of hospitalisation

Infants randomised to cup feeds had a significantly increased risk of taking longer to reach all sucking feeds (adjusted HR 1.75, 95% CI 1.34 to 2.28, P<0.001). Infants randomised to cup feeds also had a significantly increased risk of a longer duration of hospitalisation (HR 1.41, 95% CI 1.09 to 1.82, P=0.01).

8.1.3.1 Comparison with findings from other studies

Breast feeding prevalence in Australian neonatal units

Comparisons between breast feeding outcomes within Australia are problematic due to differences in reporting. Breast feeding prevalence on discharge home in the study reported in this thesis was higher than currently reported prevalence in Australian neonatal units. 71% of infants in this study were discharged home breast feeding, 53% fully breast feeding and 17% partially breast feeding. Reported proportions for any (fully and partially combined) breast feeding on discharge home from other Australian neonatal units include 54% for infants <1500 grams (Doherty and Sparkman 1997), 62% for infants less than 33

weeks gestation at birth (Simmer et al. 1997) and 64% for infants less than 35 weeks (45% exclusive and 19% partial) (Yip et al. 1996).

Studies of interventions in transition to breast feeds for preterm infants

The three published randomised controlled trials of interventions in the transition to breast feeds for preterm infants have conflicting results (Kliethermes et al. 1999; Mosley et al. 2001; Rocha et al. 2002). Kliethermes et al. (1999) found a much greater effect on breast feeding outcomes in their study comparing nasogastric tube supplementation and bottle feeds in the transition to breast feeds. Infants randomised to nasogastric tube supplementation were 4.5 times more likely to be breast feeding on discharge home (OR 4.5, 95% CI 1.4 to 15, P=0.0001). The odds ratio of going home fully breast feeding in the tube group were 9.4 (95% CI 3.1 to 28.4). Cup feeding was used in their study only during the 'rooming-in' period prior to discharge when the nasogastric tube had been removed and a supplementary feed was necessary based on weight loss. The two trials comparing cup and bottle in the transition to breast feeds, found no difference in any breast feeding (fully and partially combined) (Rocha et al. 2002) or exclusive breast feeding (Mosley et al. 2001).

The study reported in this thesis supports the work of Kliethermes et al. (1999) for infants discharged home fully breast feeding. It adds weight to the hypothesis that using bottles during the transition to breast feeds interferes with a preterm infants ability to breast feed.

Time to full sucking feeds

Time taken to reach all sucking feeds was not reported by Kliethermes et al. (1999), Mosley et al. (2001) or Rocha et al. (2002). This is, however, a marker for discharge home, the established criteria for physiologically stable preterm infants to be discharged home is that they are on all sucking feeds.

Duration of hospitalisation

In the study of Kliethermes et al. (1999) both groups had similar lengths of hospitalisation, the tube group had a mean length of stay of 35 days and the Bottle group 33 days (P=0.68). Length of hospital stay was not reported in the studies of Rocha et al. (2002) or Mosley et al. (2001). In the study reported in this thesis infants randomised to the cup group were more likely to have a longer duration of hospitalisation, with a median length of stay of 59 days compared to Bottle groups of 48 days (HR 1.41, 95% CI 1.09 to 1.82, P=0.01).

8.2 *Possible mechanisms and explanation*

8.2.1 Differences between Dummy and Bottle

Why does using a bottle make a difference to breast feeding outcomes but using dummies does not? There is a difference in sucking behaviour depending on whether it is nutritive or non nutritive. With dummy use the sucking action is non nutritive and is characterised by bursts of rapid sucks followed by pauses (Daniels et al. 1986; Hafstrom and Kjellmer 2000; Hafstrom and Kjellmer 2001). In nutritive sucking the sucking bursts are longer than the sucking pauses, and there is a slower sucking rate (Daniels et al. 1986). However, nutritive and non nutritive sucking appears to be more a function of the presence or absence of milk flow. Both a dummy teat and bottle teat reaches the hard palate only, whereas the breast extends deeper to the junction of the hard and soft palate. Bu'Lock et al. (1990) showed that tongue movements were similar between nutritive and non nutritive sucking and that swallowing was rarely observed during non nutritive sucking. Given the results of the study reported in this thesis, infants are able to adapt the mouth action and tongue position required between breast feeding and non nutritive sucking on a dummy.

The results from the study reported in this thesis and from the study of Kliethermes et al. (1999) suggest that the improvement in breast feeding outcomes occurred because bottles were not used in the transition to all breast feeds, rather than by the use of cup or tube feeds per se. In other words it is possible that not introducing a preterm infant to bottle feeds during their transition to full breast feeds improves breast feeding outcomes, regardless of the alternate method used to supplement or complement feeds.

There is substantial evidence (Meier and Anderson 1987; Meier 1988; Meier et al. 1991; Bier et al. 1993; Young 1995; Bier et al. 1997; Chen et al. 2000) demonstrating that preterm infants have higher oxygen saturation rates when breast feeding than when bottle feeding, suggesting it is easier for them to coordinate sucking, swallowing and breathing with breast feeding. It cannot, therefore, be the adverse physiological effects of bottle feeding that interfere with breast feeding outcomes. Many infants do manage to breast feed successfully when bottles have been used; 47% (n=72) of the infants randomised to bottle feeds were fully breast feeding and 68% (n=103) 'any' breast feeding on discharge home in the study reported in this thesis. The majority of infants adapt to any differences required in mouth and sucking action between the bottle and breast.

Given that:

1. this study showed no difference in breast feeding outcomes with dummy use,
2. in Klicthermes et al. (1999) study dummies were available for use in both groups, and
3. infants use the same tongue action for bottle and dummy teats, but with a different rate of sucking (Bu'Lock et al. 1990),

it is possible that the major contributing factor to bottles interfering with breast feeding outcomes is the immediate and consistent reward of milk that occurs with bottle feeds and not due to differences in sucking action between breast and bottle/dummy use.

8.2.2 Duration of hospitalisation

It is unclear why infants randomised to the cup groups took significantly longer to reach all sucking feeds and consequently had a longer period of hospitalisation. This finding was in contrast to the findings of Kliethermes et al. (1990) who found no difference in length of hospital stay. One of the main criteria for discharge home is that infants can manage all sucking feeds. As the infants matured, some became less satisfied with cup feeds and more difficult to feed by this method, this generally occurred in their last week in hospital. If the mother was unable to be present for the feed, the feed was given by gavage tube, thus delaying the onset of all sucking feeds. Reliable data were not collected on this, so it is unknown how much this may have contributed to the increased length of stay.

The increased length of stay for those randomised to cup feeds requires further investigation. In her book on breast feeding special care babies, Lang (1997) suggests that as the preterm infant matures they may be able to bottle feed without this interfering with breast feeds, but she cautions that the introduction of a bottle should only occur when breast feeding is well established. Further research is required on this hypothesis, it may be possible that such a strategy with the introduction of bottles once breast feeding is established may reduce the increased length of hospitalisation seen with the results reported in this thesis for infants cup fed.

If the increased length of hospitalisation is confirmed by further studies, alternate management practices may be appropriate which would lessen the financial impact on the health system. For example early discharge programs may be used, that enable the mother and her infant/s to be discharged home while still requiring gavage feeds (Collins et al.

2003). Such programs provide health professional support with daily, or as needed, visits by midwives skilled in the care of preterm infants until full sucking feeds are reached.

8.3 Limitations

8.3.1 Compliance

A major limitation of the study reported in this thesis is the high rate of non compliance. Of the 151 infants randomised to the cup groups 85 (56%) had a bottle introduced. 47 (31%) of the 152 infants randomised to No Dummy had a dummy introduced. Five (3%) of the 151 infants randomised to receive a dummy did not have one and one (0.7%) infant randomised to receive a bottle had a cup introduced.

Compliance in the study by Rocha et al. (2002) was high, with only one infant withdrawn from the study for not complying with the study protocol. Their nursing team was trained in cup-feeding technique and staff commitment was obtained. The involvement of the parents is not clear from their study.

In two randomised controlled trials of artificial teats and breast feeding outcomes conducted in the term infant population compliance was problematic. Schubiger et al. (1997) examined the effect of supplemental feeds and use of bottles and dummies in term newborns. The experimental group received supplements (by cup or spoon) only if medically indicated, and no bottles or dummies were allowed. The control group received standard care whereby supplements were routinely offered by bottle after each breast feed, and dummies were offered to all infants. 24% (n=70) of the experimental group introduced a dummy, 10% (n=28) used a bottle for supplementary feeds.

Kramer et al. (2001a) tested whether dummy use was causally related to weaning in term infants. Participants were randomly allocated to one of two counselling interventions, the experimental group were recommended to avoid the use of a dummy and alternate ways of comforting their infant were suggested. For the control group dummy use was recommended as one of the options for calming their infant. Dummy use was significantly reduced in the experimental group, however a substantial proportion (61.4%) still used a dummy compared to 84% in the control group.

Compliance in the study reported in this thesis differed between the two participating recruiting centres. Those recruited at the WCH had a far higher rate of non compliance than the MHW. 66% (n=36) of infants recruited at the WCH had a bottle introduced compared to 51% (n=49) at the MHW; 57% (n=29) of infants recruited at the WCH had a dummy introduced compared to 18% (n=18) at the MHW. The introduction of bottles or dummies could occur at the recruiting or peripheral hospital, 54 peripheral hospitals participated in the study. Unfortunately, data were collected in such a way as to be unable to determine with confidence where the protocol breach occurred.

Experience with cup feeding would be a contributing factor to compliance. The MHW had been cup feeding in their neonatal unit for approximately three years before the study began. Cup feeding was only introduced to the WCH specifically for the randomised controlled trial and the majority of the peripheral hospitals did not use cup feeding before this study.

Support for the staff at the WCH and MHW included in-service education, written instructions, supporting literature, one-to-one support where needed before commencing the trial and during the trial. Written instructions and supporting literature were available to all participating peripheral hospitals. An in-service education session was given to the metropolitan hospitals participating in the Adelaide area, along with telephone support. Support for South Australian country hospitals was by telephone only. Support for participating Victorian peripheral hospitals was by telephone and written information only.

Some staff had very strong feelings against cup feeding and the withholding of dummies and directly influenced parents; some staff refused to cup feed. Feedback from some staff during the study was that they felt uncomfortable and unfamiliar with cup feeding. In contrast the one mother who changed from bottle to cup did so because she was transferred to a peripheral hospital where cup feeding of preterm infants was the norm, she saw all the other mothers and staff cup feeding and was influenced by this. Some parents did not like cup feeding and felt that their infant needed to use a bottle to 'learn' how to suck. The trial also did not have great appeal to parents with 37% of the 442 mothers approached not wanting to participate.

Sackett (2000) states that one reason why randomised controlled trials fail is failure to gain commitment at the "coal-face". The principle underlying "coal-face" commitment is that

'only clinicians and patient who consider an RCT "theirs" should be expected to follow its protocol' (Sackett 2000, p. 1313). While this study had the support of the neonatal and midwifery heads of departments, the "coal-face" support was not as strong as was needed to ensure good staff support for the interventions.

Trials are undertaken for alternative treatments when clinicians are uncertain about whether their opinions on the treatment are correct, Sackett calls this the *'uncertainty principle'* (Sackett 2000). However clinicians can be so convinced of the experimental treatments efficaciousness, or uselessness, that they refuse to participate in the trial (Sackett 2000). Although not formally studied few of the staff held enough of the "uncertainty principle" about cup feeding and withholding a dummy, many staff believing strongly that the experimental treatment was ineffective. With better support and more involvement with the trial development these views and, therefore, compliance may have been different.

A systematic literature review of clinician and patient barriers to participation, including barriers to protocol adherence as well as barriers to taking part in trials, has been undertaken by Ross (1999). The barriers to clinician participation identified included time constraints, lack of staff and training, worry about the impact on clinician-patient relationship (in particular admitting they don't know which treatment is best), concern for patients, loss of professional autonomy, and an insufficiently interesting research question. Barriers to patient participation include additional demands on the patient, preferences for a particular treatment or no treatment, worry about uncertainty of treatment or trials, and the clinician as a barrier to patient participation. Clinicians may act as a barrier to patient participation when there is an incompatibility of the study protocol with usual practice, this includes a clinician's personal preference for one of the treatments. This can lead to the clinician influencing the patient decision not to join (Ross et al. 1999), or, on extrapolation, clinician preference would also influence patient adherence to the protocol.

Due to financial limitations peripheral hospitals did not receive comprehensive support. Time and financial constraints also limited the amount of support available to the recruiting hospitals, the amount of support staff actually needed was underestimated. Experience from a neonatal unit advises that cup feeding be introduced slowly to prevent staff opposition (Musoke 1990). Staff feelings were such that, even in the unit where cup feeding had been practiced for several years, some were still very opposed.

The study reported in this thesis was designed as a 'pragmatic' or 'management' trial. It was clinically oriented to answer the question would the interventions of cup feeding and withholding a dummy, when managed by a wide range of clinicians and not necessarily taken up by patients, increase the prevalence of breast feeding. In an 'explanatory' or 'efficacy' trial the aim is to find out the effect of the intervention in ideal circumstances, in participants who do receive and maintain compliance. Even so, measures should be taken to gain compliance in pragmatic trials as high rates of non compliance make interpretation difficult (Haynes and Dantes 1987). In this study, the efficacy of cup feeding and not using a dummy is unable to be confidently determined due to the high non compliance. High non compliance causes a considerable dilution of the effect suggesting that the results would be greater if compliance were higher. It remains unknown, therefore, if the lack of benefit for 'any' breast feeding is due to the lack of compliance or to lack of efficacy.

8.3.2 Bias

A further limitation of the study is the possibility for introduction of bias by the unblinded nature of the study. It was not possible to blind participants and their carers to the research allocation. Due to the financial limitations of the study it was not possible to blind the study investigator to study allocation. Recruitment, trial and hospital data collection for the WCH and participating centres were undertaken by the study investigator, and by a research midwife at the MHW and participating centres. The three and six month questionnaires were administered and followed up by the study investigator. The study investigator also entered the data and undertook the analysis. Data entry could not be done blinded to study group, however, it would have been possible to undertake the data analysis blinded to study group. Not doing so is a limitation of the study.

8.4 Clinical and public health implications

This study provides no evidence to support not using a dummy in preterm infants less than 34 weeks gestation as a strategy to increase breast feeding prevalence. It also provides strong evidence that using a dummy does not accelerate sucking maturation or length of hospital stay. Infants have an innate need to suck, dummies can safely be used for preterm infants during hospitalisation without fear of interfering with breast feeding outcomes.

In this study with nearly half of the participants non compliant, the use of cups significantly increased the proportion of infants discharged home fully breast feeding

compared with partially and not breast feeding. If the desired outcome is fully breast feeding on discharge home then the use of cups is beneficial. The increase in those fully breast feeding needs to be tempered with the results that the use of cups significantly increased the risk of an increased time to full sucking feeds and hospital stay and the consequent financial implications for the health system.

There is a beneficial health effect for preterm infants in receiving any breast milk, the outcome 'any breast feeding' is therefore important. This study was unable to show a difference in the proportion of infants discharged home breast feeding (fully or partially) compared to not breast feeding. It remains unknown if the lack of benefit is due to the lack of compliance or to lack of efficacy of cup feeding. The exploratory compliance analysis showed a significant increase in the odds ratio of any breast feeding, and in the risk of an increase in length of time taken to reach full sucking feeds, but showed no significant difference in length of hospital stay. Confirmation of these findings by further research is therefore necessary.

Given the difficulty in staff and parent acceptance of cup feeding in this study and the lack of effect on the outcome 'any breast feeding', it would be difficult to recommend the introduction of cup feeding into nurseries, except where staff are keen to use this modality. Processes would then need to be put in place to monitor the effect on length of hospital stay and consideration given to early discharge programs with home support of gavage feeding. This study however, adds support to the findings of Kliethermes (1999) that not introducing bottles increases breast feeding success.

8.5 Research implications

A sufficiently powered, randomised controlled trial is needed to assess if cup feeding has an effect on the outcome any breast feeding and to determine if the poor compliance, the effect on time to reach all sucking feeds and length of hospital stay was particular to this trial. Research to determine if the timing of the introduction of bottle feeds affects breast feeding outcomes is required.

Chapter 9. Protocol: Systematic Reviews

Two systematic reviews were undertaken. One systematic review reports the addition of data from the randomised controlled trial reported in this thesis to an existing review on the effect of non nutritive sucking on preterm infants, and the other compares the use of no bottles to bottles in the transition to breast feeds for preterm infants.

The systematic reviews were undertaken using the standard format of the Cochrane Collaboration as described in the Cochrane Reviewer's Handbook (Clarke et al. 2003) and the Neonatal Collaborative Review Group (Sinclair et al. 2003). Data from the study reported in this thesis were added to the existing Cochrane Review on the use of dummies in preterm infants (Pinelli and Symington 2003) as detailed in section 9.1. The protocol for conducting a systematic review of the effect on breast feeding of interventions used in the preterm infant's transition from tube to breast feeds is detailed in 9.2.

9.1 Protocol for addition of data into existing Cochrane Review

The existing Cochrane Review is titled *'Non-nutritive sucking for promoting physiologic stability and nutrition in preterm infants'*. The study reported in this thesis was assessed against Pinelli's (2003) inclusion criteria:

> **Types of studies**
> All experimental and quasi-experimental studies in which non-nutritive sucking (NNS) in preterm infants was compared to no provision of non-nutritive sucking.
>
> **Types of participants**
> All infants born at less than 37 weeks post-conceptual age.
>
> **Types of intervention**
> Non-nutritive sucking involving the use of a pacifier. The intervention occurred before, during or after feeding by a naso/orogastric tube; before or after bottle feeding; or outside of feeding time.
>
> **Types of outcome measures**
> a) weight gain, b) length of hospital stay, c) transition to oral/nipple feedings, d) heart rate and oxygen saturation/oxygenation, e) activity/behaviour, f) any other clinically relevant outcomes (Pinelli and Symington 2003).

The methodological quality of the study reported in this thesis was assessed according to criteria detailed in the systematic review (Pinelli and Symington 2003): blindness of randomisation, blindness of intervention, complete follow up, blinding of outcome measurement, evidence of co-intervention, objective criteria of measuring outcomes and

defined exclusion/inclusion criteria. Data were added to the existing meta-analyses for the outcomes length of hospital stay, weight gain and transition to oral/nipple feedings. Data were extracted from the review and entered into the MetaView component of the Cochrane Collaboration's Review Manager software (RevMan), version 4.2 (RevMan 2003).

9.2 Protocol for systematic review

9.2.1 Review title

Bottle feeding during the transition from tube to breast feeds in preterm infants.

9.2.2 Background

During a preterm infant's transition from tube to all breast feeds it is not always possible for the mother to be present to breast feed and an alternate method of supplementing and complementing sucking feeds is used, most commonly this is by bottle. It is thought that bottles may interfere with establishing successful breast feeding possibly because of a difference in sucking action required for breast and for artificial teats (Bu'Lock et al. 1990; Neifert et al. 1995). An increased breast feeding prevalence has been reported when bottle feeds have been replaced by cup feeds (Lang et al. 1994; Gupta et al. 1999) or by tube only (Stine 1990) in this transition time, however these studies were small and uncontrolled. Finger feeding a preterm infant as an alternative to bottle or cup feeds has been described in a case report (Kurokawa 1994; Healow 1995). This involves taping a size 5 FG feeding tube to the side of the finger and inserting the finger, pad side up into the infant's mouth, the feeding tube is attached to a syringe filled with milk and plunger removed, as the infant sucks milk is drawn down through the tube (Kurokawa 1994; Healow 1995).

Bottle feeding is more stressful for preterm infants when compared to breast feeding as shown in randomised (Young 1995) and non randomised crossover studies (Meier and Anderson 1987; Meier 1988; Bier et al. 1993; Bier et al. 1997) and with paired observations (Chen et al. 2000). Temperature is unchanged with breast feeding (Bier et al. 1993) or increased (Meier 1988; Meier et al. 1991; Bier et al. 1997; Chen et al. 2000). There were no significant differences in heart or respiratory rate between breast and bottle feeding (Bier et al. 1993; Bier et al. 1997; Chen et al. 2000). Desaturations (<90%) occur more frequently with bottle feeding (Bier et al. 1993; Young 1995; Bier et al. 1997; Chen et al. 2000) and mean oxygen saturation (Meier et al. 1991; Bier et al. 1997; Chen et al.

2000) and transcutaneous oxygen pressure is lower (Meier and Anderson 1987; Meier 1988).

Cup feeding has been compared to breast feeding in a non randomised cross-over study of preterm infants (Freer 1999). No significant difference was found in respiratory rate or heart rate between breast and cup feeding, however heart rate was more stable during breast feeds. There was a statistically but not clinically significant difference in the mean oxygen saturation between the two feeding methods (breast feeds mean 96% SD 2.4, Cup feeds 94%, SD 3.5). Mean breast feeding duration was longer than cup feeding, however when divided by gestational age at time of feeding the mean breast feeding time was comparable but the cup feeding time increased with increasing gestational age. In a case series Dowling (2002) described the effect of cup feeding in eight preterm infants. Breathing remained stable during cup feeds, the lowest oxygen saturation during the feed was 83% however the volume of intake was low with 39% of milk dribbled on to the bib.

For mothers who wish to breast feed their preterm infant it is important to establish the most efficacious and least harmful method of supplementing or complementing breast feeds in the transition from tube to breast feeding.

9.2.3 Objectives

The primary objective was to determine the effects of not using bottles (instead using interventions such as cup feeding, tube alone, spoon, dropper or finger feeding) during the preterm infants transition from tube to breast feeds compared with using bottles.

Subgroup analyses were planned to determine if safety and efficacy outcomes were altered by the maturity of the infants (for example, gestational age < 28 weeks at birth; 28 to <34 weeks and 34 to <37 weeks). Subgroup analyses were also planned by type of intervention (for example bottle compared to cup, bottle compared to tube alone etc).

9.2.4 Criteria for considering studies for this review

Types of Studies

All published trials using random or quasi-random patient allocation.

Types of Participants

Infants born less than 37 weeks gestation whose mother has chosen to breast feed. Infants requiring supplemental oxygen may be included.

Types of Interventions

Bottle feeding infants during the transition from tube to breast feeds versus no bottle (eg cup, tube, spoon, dropper, finger feeding). No bottle was classified as the treatment and bottle the control.

Types of Outcome measures

Primary efficacy outcomes:

1. Feeding and growth outcomes as assessed by:
   - 1.1 number of days to reach full sucking feeds
   - 1.2 breast feeding prevalence (any compared to not breast feeding and fully compared to partially and not breast feeding) on discharge home and at 3 and 6 months post discharge
   - 1.3 weight gain
   - 1.4 length of hospitalisation
   - 1.5 duration of feed

Primary safety outcomes:

2. Adverse events
   - 2.1 cardio-respiratory stability during and after intervention
   - 2.2 milk aspiration – on radiologic assessment

Secondary outcomes:

1. Satisfaction
   - 1.1 parental satisfaction as measured by self report
   - 1.2 health personnel satisfaction as measured by self report

9.2.5 Search strategy

Computerised searches were conducted of the Cochrane Central Register of Controlled Trials (Issue 1 2003), MEDLINE (1966 to May Week 3 2003), CINAHL (1982 to April Week 1 2003) and EMBASE (1980 to 2003 Week 15). The MeSH headings used were:

Breast feeding; Milk, human; Infant, Newborn; Infant, Newborn, Diseases; Intubation, Gastrointestinal. The following text words were used: Neonat$, Cup, Cup Fe?d$, Cupfe?d$, Gavage, Gavage feed$, Tube feed$, Spoon, Dropper, Finger Fe?d$.

To identify randomised controlled trials or controlled clinical trials, the following search strategy, developed by Carol Lefebvre of the United Kingdom Cochrane Centre, was used for OVID MEDLINE (The Editorial Team 2003).

1. randomized controlled trial.pt.
2. randomized controlled trials/
3. controlled clinical trial.pt.
4. random allocation/
5. double blind method/
6. single-blind method/
7. or/1-6
8. clinical trial.pt.
9. exp clinical trials/
10. (clin$ adj25 trial$).tw.
11. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).tw.
12. placebos/
13. placebo$.tw.
14. random$.tw.
15. research design/
16. or/8-15
17. comparative study/
18. exp evaluation studies/
19. follow up studies/
20. prospective studies/
21. (control$ or prospectiv$ or volunteer$).tw.
22. or/17-21
23. animal/ not (human/ and animal/)
24. 7 or 16 or 22
25. 24 not 23

To identify randomised controlled trials or controlled clinical trials in Ovid CINAHL and Ovid EMBASE the following MeSH terms were used: randomised controlled trials, random allocation, double blind method, single-blind method, clinical trials.

The search was not restricted by language.

9.2.6 Methods of the review

Standard methods of the Cochrane Collaboration (Clarke et al. 2003) and the Cochrane Neonatal Review Group were used (Sinclair et al. 2003).

Selection of studies for inclusion

Studies were excluded if it was apparent from the abstract that they did not meet the inclusion criteria. Where there was uncertainty about inclusion of the study, the full text was retrieved.

Assessment of methodological quality

Once inclusion of trials was established, the methodology of the trial was assessed. The data were extracted onto hard copy data sheets and data extraction and quality assessment was undertaken. The standard review method of the Neonatal Review Group (Sinclair et al. 2003) was used to assess the methodological quality of the included trials. This included assessing the trial for blinding of randomisation or allocation concealment, blinding of intervention, completeness of follow up and blinding of outcome measurement. Results of assessment were reported as 'Yes', 'Can't tell', or 'No'. In addition each trial was assigned a quality rating for allocation concealment (Clarke et al. 2003). 'A' indicates that allocation concealment was adequate (for example telephone randomisation, or use of consecutively numbered, sealed, opaque envelopes), 'B' unclear (for example not reported or unclear), and 'C' inadequate if the method was not convincing of concealment (for example, coin toss at enrolment, open random number lists or quasi-randomisation such as alternate days, hospital number of date or odd/even date of birth) (Clarke et al. 2003).

Additional information was requested from Kliethermes (1999), Malhotra (1999) and Rocha (2002) to clarify methodology and seek further data regarding outcomes.

Analysis

Data were entered into the MetaView component of the Cochrane Collaboration's Review Manager software (RevMan), version 4.2 (RevMan 2003). Analysis was by intention-to-treat. For categorical data the proportion of participants experiencing the outcomes in the experimental and control group were extracted and entered into MetaView. Relative risk (RR) and risk difference (RD) with 95% confidence intervals were calculated. For continuous data the mean and standard deviations (SD) for the experimental and control groups were extracted and entered into MetaView. Weighted mean difference (WMD) with 95% confidence intervals were calculated. The Neonatal Review Group state that to test for heterogeneity between trials a standard chi squared test, with significance defined as $P<0.05$, is used (Sinclair et al. 2003). However, Cochrane Reviews have recently introduced a new measure of the consistency between trials, the I^2 statistic, which describes the percentage of total variation across studies that is due to heterogeneity rather than chance (Higgins and Thompson 2002; Higgins et al. 2003). An I^2 value of 25% is considered indicative of low inconsistency, 50% moderate and 75% high (Higgins et al. 2003). Heterogeneity was explored when I^2 was 50% or greater. Meta-analysis was performed using a fixed effects model.

Chapter 10. Systematic Reviews

10.1 Addition of data into existing Cochrane Review: 'Non-nutritive sucking for promoting physiologic stability and nutrition in preterm infants' (Pinelli, 2003).

See Chapter 9 (section 9.1) for the protocol on addition of data from the study reported in this thesis to the existing Cochrane Review.

10.1.1 Eligibility for inclusion

The study reported in this thesis was eligible for inclusion in the existing Cochrane Systematic Review (Pinelli and Symington 2003) as assessed against their eligibility criteria:

> **Types of studies:** All experimental and quasi-experimental studies in which non-nutritive sucking (NNS) in preterm infants was compared to no provision of non-nutritive sucking (Pinelli and Symington 2003).

The study was an experimental study in which non-nutritive sucking in preterm infants was compared to no provision of non nutritive sucking.

> **Types of participants:** All infants born at less than 37 weeks post-conceptual age (Pinelli and Symington 2003).

The infants included in the study were born at less than 34 weeks gestation.

> **Types of intervention:** Non-nutritive sucking involving the use of a pacifier. The intervention occurred before, during or after feeding by a naso/oro-gastric tube; before or after bottle feeding; or outside of feeding time (Pinelli and Symington 2003).

Non nutritive sucking for the study involved use of a dummy (pacifier) available at all the above time points.

> **Types of outcome measures:** a) weight gain, b) length of hospital stay, c) transition to oral/nipple feedings, d) heart rate and oxygen saturation/oxygenation, e) activity/behaviour, f) any other clinically relevant outcomes (Pinelli and Symington 2003).

The outcome measures from the study can be included are weight gain, length of hospital stay, transition to oral/nipple feedings and effect on breast feeding.

10.1.2 Methodological quality

The study reported in this thesis was assessed against the criteria used in the systematic review (Pinelli and Symington 2003):

Blindness of randomisation: yes
Blindness of intervention: no, not possible
Complete follow-up: 319 randomised, 16 post randomisation exclusions (12 died, 4 withdrew)
Blinding of outcome measurement: no
Objective criteria of measuring outcomes: yes
Defined exclusion/inclusion criteria: yes

Infants in the study were randomised to cup/no dummy, cup/dummy, bottle/no dummy, bottle/dummy; there was no statistically significant interaction between no dummy use and cup and therefore results from the marginal groups No dummy versus Dummy were able to be added to Pinelli et al. (2003) systematic review.

An intention to treat analysis was undertaken. There was a high proportion of non compliance, five (3%) of the 151 infants randomised to receive non nutritive sucking did not, and 47 (31%) of the 152 infants randomised to not have non nutritive sucking with a dummy had a dummy introduced.

10.1.3 Results

10.1.3.1 Weight gain

Pinelli et al. (2003) included three randomised controlled trials (Field et al. 1982; Ernst et al. 1989; Mattes et al. 1996) in the meta-analysis for the outcome weight gain (grams/day) and showed a non significant overall effect (WMD 1.57 g/day, 95% CI - 0.37 to 3.50). A statistically and clinically non significant effect on weight gain remained with the addition of data reported in this thesis (WMD –0.22 g/day, 95% CI -1.34 to 0.90) (Figure 10.1). However, there is now a moderate degree of heterogeneity among trials (chi square=6.58, df=3, P=0.09, I^2=54.4%).

The trials differed in the administration of the intervention, one of the trials included in the meta-analysis (Field et al. 1982) allowed use of a dummy between feeds for both the experimental and control groups and another trial did not report whether dummies were available between feeds. In the trial of Ernst et al. (1989) dummies were not allowed between feeds for the experimental or the control groups, whereas in the trial reported in this thesis (Collins 2003) dummies were not allowed at any time for the experimental groups and were allowed at all times for the control groups. There is now no heterogeneity ($Chi^2 = 0.86$, df = 1 (P = 0.35), $I^2 = 0\%$) and there remains a clinically and statistically non significant difference in weight gain (WMD –0.85 g/day, 95% CI –2.10 to 0.41) in the subgroup of two trials that are most similar in terms of administration of the intervention (Ernst et al. 1989; Collins 2003) (Figure 10.2).

In terms of quality of study, allocation concealment was adequate in two trials (Mattes et al. 1996; Collins 2003). There is now no heterogeneity ($Chi^2 = 0.86$, df = 1 (P = 0.35), $I^2 = 0\%$) and there remains a clinically and statistically non significant difference in weight gain (WMD –1.08 g/day, 95% CI –2.42 to 0.26) in the subgroup of two highest quality trials (Figure 10.3).

10.1.3.2 Length of hospital stay

Pinelli et al. (2003) included two trials (Field et al. 1982; Bernbaum et al. 1983) in the meta-analysis for the outcome length of hospital stay (days) which showed a significant overall reduction in hospital stay (WMD –7.1 days, 95% CI –12.6 to –1.7) for those randomised to non nutritive sucking. With the addition of data from the study reported in this thesis (Collins 2003) the effect on hospital stay was now not significant (WMD -3.97 days, 95% CI -8.10 to 0.15) (Figure 10.4).

'Time to event' outcomes (length of hospital stay and transition to oral/nipple feeds) in the Pinelli et al. (2003) systematic review have been reported using the arithmetic mean and standard deviations. A more appropriate method of analysis for 'time to event' data is survival analysis. Survival analysis uses information from all participants including those who have not reached the 'event', in this case discharge home. Thus, data for infants who died or withdrew from the study are able to be used. As the arithmetic mean has been used in the systematic review, data from the study reported in this thesis was also reported in this manner, excluding infants who died and withdrew from the study (n=16). The

survivorship mean (censoring for infants who died, withdrew and for whom final discharge date were missing, at the time of last available data, n=18) and arithmetic mean were very similar (Dummy: survivorship mean 57.77 days, standard error (SE) 2.30, 95% CI 53.26 to 62.58; arithmetic mean 57.21 days, SD 28.15; No Dummy survivorship mean 58.17 days, SE 2.44, 95% CI 53.40 to 62.95; arithmetic mean 56.95 days, SD 27.58).

10.1.3.3 Transition time to oral/nipple feedings

The trials included in Pinelli et al. (2003) systematic review measured the effect non nutritive sucking had on the time taken to reach all bottle feeds. A meta-analysis was not performed. Pinelli et al. (2003) reports on the results from Field et al. (1982) and Sehgal et al. (1990). Field et al. (1982) found a 3 day reduction in days of tube feeding (P=0.01) with non nutritive sucking, it is unclear if they measured the number of days from the first tube feed or days from birth. Seghal et al. (1990) found a 1.6 day difference in the time between total gavage and total bottle feeds (P<0.001). The study reported in this thesis measured the time (days) taken to reach all sucking feeds (bottle or breast) from birth to last gavage tube feed. No significant benefit was found with non nutritive sucking (MD –1.03 days, 95% CI –6.87 to 4.81) (Figure 10.5). The survivorship mean was very similar to the arithmetic mean (Dummy: survivorship mean 47.63 days, SE 2.09, 95% CI 43.526 to 51.73; arithmetic mean 47.24 days, SD 24.72; No Dummy survivorship mean 48.44 days, SE 2.10, 95% CI 44.32 to 52.56; arithmetic mean 48.27 days, SD 26.05).

Mattes et al. (1996) showed no significant difference in the mean age for tolerance of full oral feeds, interestingly reported as the number of days from conception (NNS n=13, 249.7 days, SD 62.08, No NNS n=11, 251.4 days, SD 57.6). By converting the gestational age at birth into days of gestation and adding the number of days to last gavage feed, it was possible to add data from the study reported in this thesis (Collins 2003) to the meta-analysis (Figure 10.6). There remained no significant effect of non nutritive sucking on days to full oral feeds (WMD –1.32 days, 95% CI –4.32 to 1.58).

10.1.3.4 Displaying results for breast feeding outcomes

The convention in the Cochrane Collaboration for presenting results is:

> ...if the odds ratio or relative risk for unfavourable dichotomous outcomes is less than one, (and risk differences are less the zero), this indicates that the treatment is better than the

> control. This is represented in the graphs by estimates to the left of the vertical line that indicates no difference (Clarke et al. 2003, p. 67).

However they also recognise that there are circumstances where it may be inappropriate to show 'bad' outcomes.

> It sometimes makes more sense to present the results for 'good' outcomes; for example livebirth after treatment for infertility instead of 'no livebirth', or smoking cessation after an intervention to help people to quit smoking instead of 'failure to quit smoking' (Clarke et al. 2003, p. 68).

The breast feeding results for the systematic review reported in this thesis are therefore presented as a 'good outcome', that is, 'any breast feeding' or 'fully breast feeding' instead of 'not any breast feeding' or 'not fully breast feeding'.

10.1.3.5 Effect on breast feeding

The effect on breast feeding was not included as an outcome in Pinelli et al. (2003) systematic review. The outcome 'any breast feeding' is defined as a combined group of fully and partially breast feeding compared to not breast feeding, and the outcome 'fully breast feeding' is compared to a combined group of partially and not breast feeding. The inclusion of data from the study reported in this thesis (Collins 2003) in the review shows a non significant effect of non nutritive sucking on breast feeding prevalence (any or fully) on discharge home (Figure 10.7), and at three and six months post discharge (Figure 10.8 and Figure 10.9).

For the study reported in this thesis, Labbok and Krasovec's (1990) definition for fully breast feeding for discharge home was used (defined as giving no other solid or liquid apart from vitamins, minerals, water, juice or ritualistic feeds given infrequently in addition to breast feeds). Infants who on discharge home were receiving complementary or supplementary feeds of breast milk were considered as fully breast fed. At three and six months post discharge the term 'all breast feeds' was used to represent that the infant's milk feeds were only breast feeds with no other types of milk given, 'partial' meaning that the infant's milk feeds were a combination of breast feeds and other types of milk. The intent was to determine the type of milk feeds infants were receiving (breast or formula) irrespective of whether they were receiving solids. This does not fit with the accepted definition of full breast feeding (Labbok and Krasovec 1990), that is, if an infant is on solids and all milk feeds are breast feeds they are classified as partially breast feeding. The

prevalence for 'all breast feeds' cannot therefore be combined with fully breast feeding reported in other studies and are therefore reported in the text and not included in Meta View: all breast feeds at 3 months post discharge NNS n=34/141, 24%; No NNS n=44/142, 31%; all breast feeds at 6 months post discharge NNS n=23/140, 16%; No NNS 34/141, 24%.

10.1.4 Discussion

The results of Pinelli et al. (2003) systematic review demonstrated a significant benefit of non nutritive sucking on reducing length of hospital stay. The addition of data reported in this thesis to the review now shows the effect of non nutritive sucking on length of hospital stay to be non significant. A non significant effect on weight gain (grams/day) remains. A meta-analysis was not possible for transition from tube to bottle feeds due differences in reporting. A non significant effect on post-conceptual age at full oral feeds remains. Non nutritive sucking has no significant effect on breast feeding prevalence on discharge home and at three and six months post discharge.

10.1.5 Conclusions

Implications for practice

The results from the addition of data reported in this thesis to Pinelli et al. (2003) systematic review indicate that non nutritive sucking has no significant effect on weight gain, length of hospital stay, transition to full sucking feeds and breast feeding prevalence. Given the positive behavioural effects reported in Pinelli et al. (2003) review and the absence of any negative effects non nutritive sucking on a dummy can be safely used by preterm infants.

Implications for research

It would be useful to confirm these findings in a well designed, sufficiently powered randomised controlled trial. Outcome measures need to be clearly defined and reported. It is recommended that time to full oral feeds be reported as days from birth to last gavage feed. Breast feeding needs to be clearly defined to allow comparisons.

10.1.6 MetaView Graphs

Figure 10.1 Weight gain, NNS versus No NNS

Review: Non-nutritive sucking (NNS) for promotion of physiologic stability and nutrition in preterm infants (Pinelli 2003)
Comparison: Non nutritive sucking versus no non nutritive sucking
Outcome: Weight gain (grams/day)

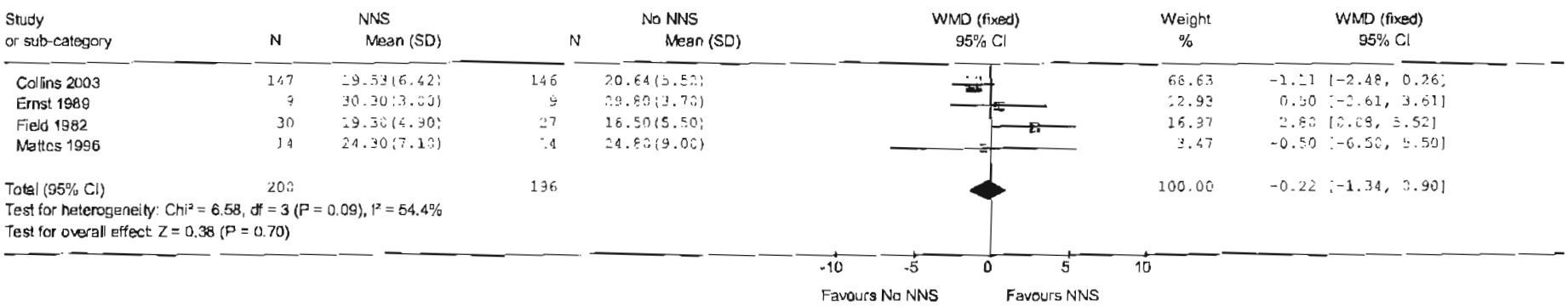


Figure 10.2 Weight gain, NNS versus No NNS, subgroup analysis by intervention

Review: Non-nutritive sucking (NNS) for promotion of physiologic stability and nutrition in preterm infants (Pinelli 2003)
Comparison: Studies with most similar intervention
Outcome: Weight gain (grams/day)

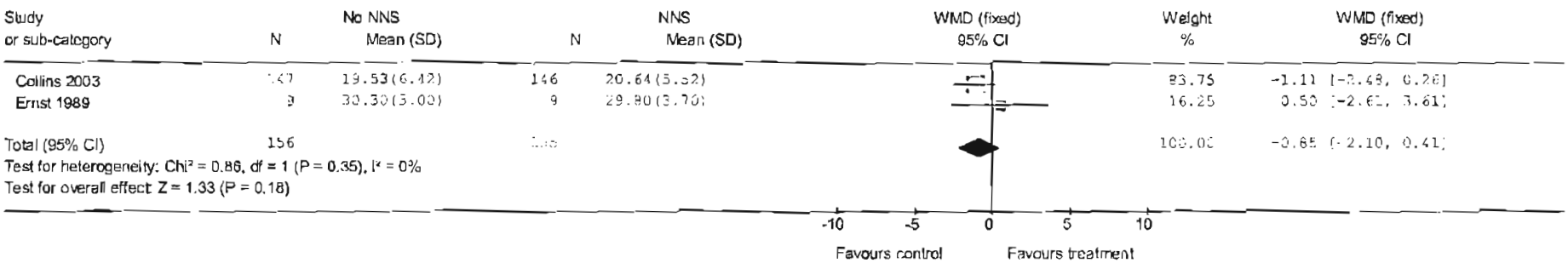


Figure 10.3 Weight gain, NNS versus No NNS, subgroup analysis by trial quality

Review: Non-nutritive sucking (NNS) for promotion of physiologic stability and nutrition in preterm infants (Pinelli 2003)
Comparison: Sensitivity analyses
Outcome: Weight gain (C, M)

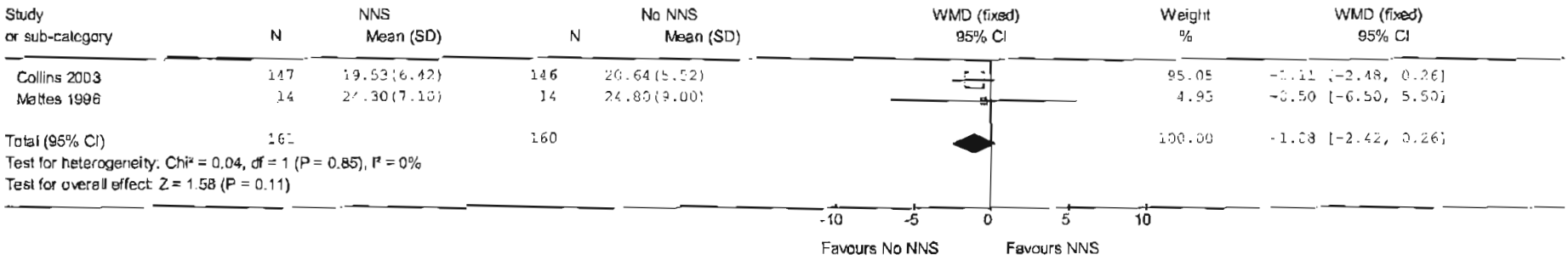


Figure 10.4 Length of hospital stay, NNS versus No NNS

Review: Non-nutritive sucking (NNS) for promotion of physiologic stability and nutrition in preterm infants (Pinelli 2003)
Comparison: Non nutritive sucking versus no non nutritive sucking
Outcome: Length of hospital stay

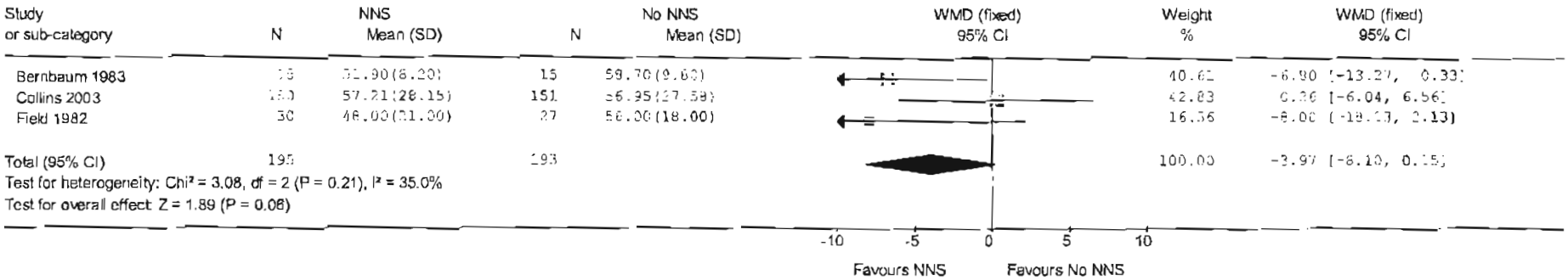


Figure 10.5 Days from birth to last gavage feed, NNS versus No NNS

Review: Non-nutritive sucking (NNS) for promotion of physiologic stability and nutrition in preterm infants (Pinelli 2003)
Comparison: Non nutritive sucking versus no non nutritive sucking
Outcome: Days from birth to last gavage feed

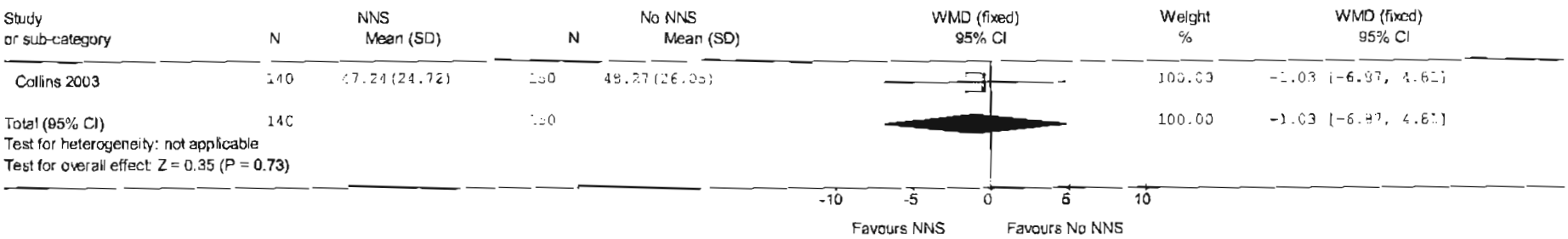


Figure 10.6 Post-conceptual age at full oral feeds (days), NNS versus No NNS

Review: Non-nutritive sucking (NNS) for promotion of physiologic stability and nutrition in preterm infants (Pinelli 2003)
Comparison: Non nutritive sucking versus no non nutritive sucking
Outcome: Post-conceptual age at full oral feeds (days)

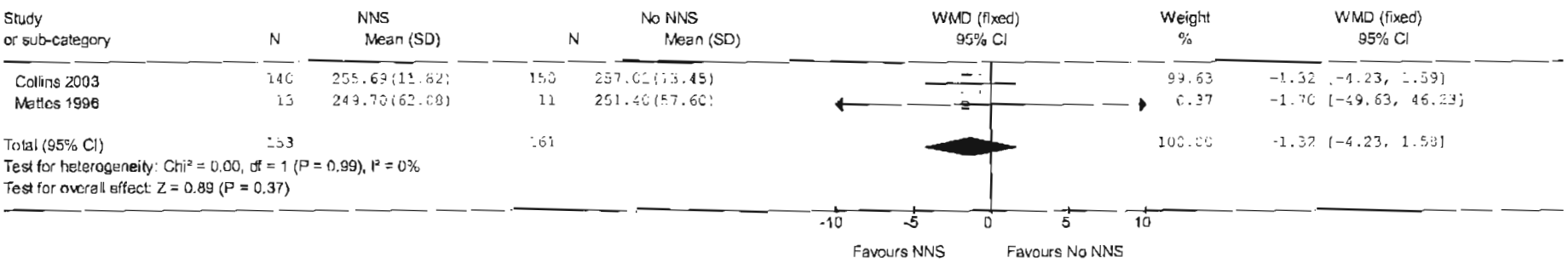


Figure 10.7 Breast feeding on discharge home, NNS versus No NNS

Review: Non-nutritive sucking (NNS) for promotion of physiologic stability and nutrition in preterm infants (Pinelli 2003)
Comparison: Non nutritive sucking versus no non nutritive sucking
Outcome: Breast feeding on discharge home

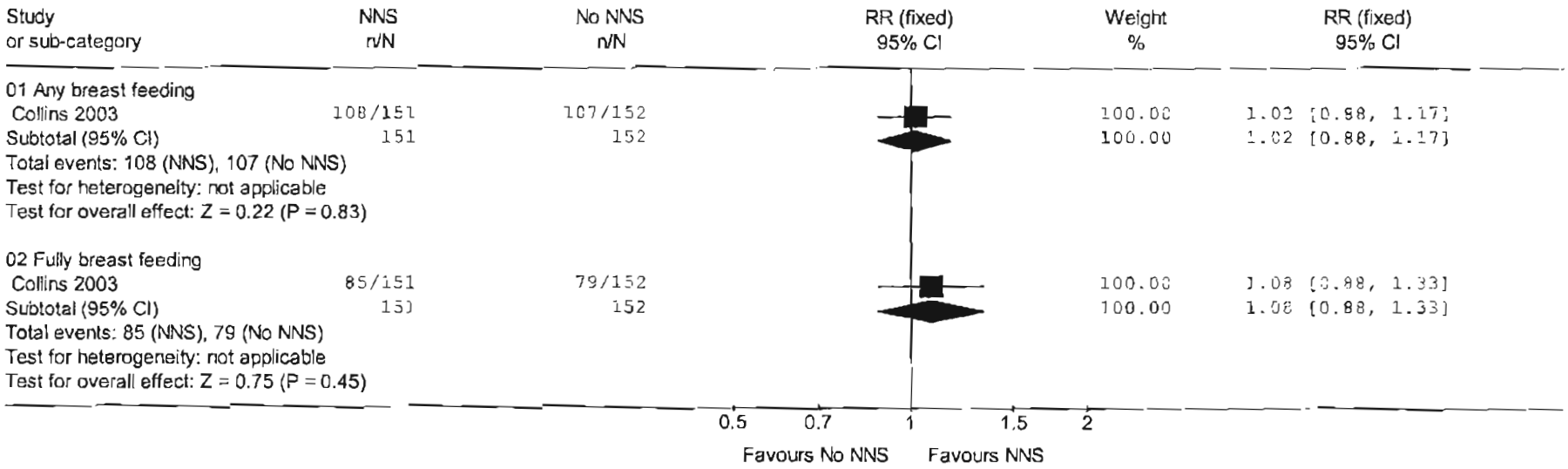


Figure 10.8 Any breast feeding at three months post discharge, NNS versus No NNS

Review: Non-nutritive sucking (NNS) for promotion of physiologic stability and nutrition in preterm infants (Pinelli 2003)
Comparison: Non nutritive sucking versus no non nutritive sucking
Outcome: Any breast feeding at 3 months post discharge

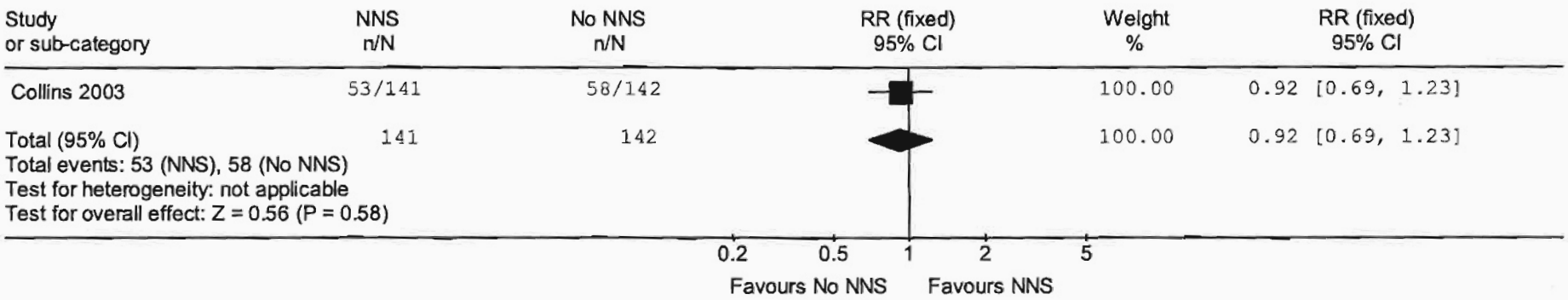
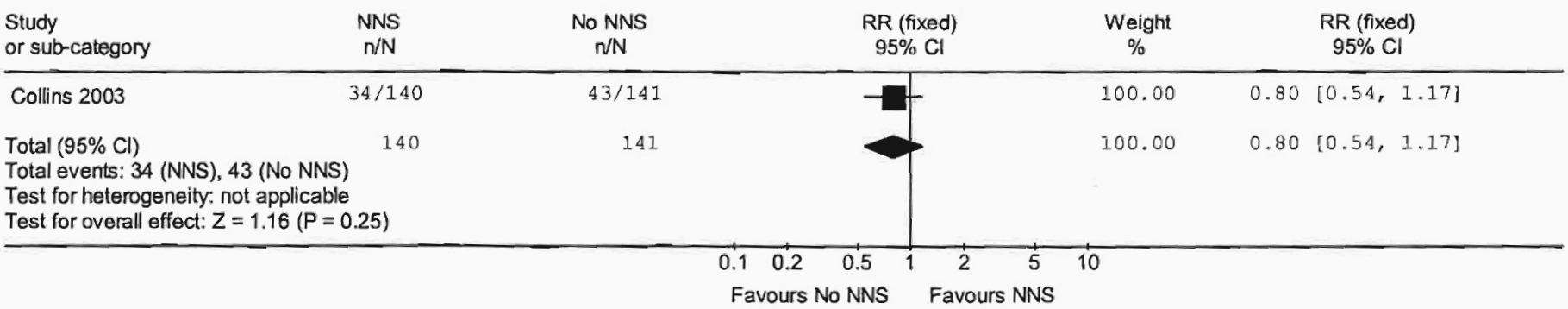


Figure 10.9 Any breast feeding at 6 months post discharge, NNS versus No NNS

Review: Non-nutritive sucking (NNS) for promotion of physiologic stability and nutrition in preterm infants (Pinelli 2003)
Comparison: Non nutritive sucking versus no non nutritive sucking
Outcome: Any breast feeding at 6 months post discharge



10.2 Systematic Review "Bottle feeding during the transition from tube to breast feeds in preterm infants".

See Chapter 9 (section 9.2) for the protocol for this systematic review.

10.2.1 Description of studies

Thirteen trials were identified, five trials were included in the review and eight excluded.

10.2.1.1 Included studies

Five studies were included in this review, details of each of the included studies (Kliethermes et al. 1999; Marinelli et al. 2001; Mosley et al. 2001; Rocha et al. 2002; Collins 2003) are given in the Characteristics of Included Studies (section 10.2.7).

10.2.1.1.1 Participants

All of the included studies except the study reported in this thesis (Collins 2003) were single centre. The total number of infants after post randomisation exclusions in each study varied from 14 (Mosley et al. 2001) to 303 (Collins 2003). All studies included preterm infants although the limits for gestational age at birth or birthweight differed. Two studies had no lower limit for gestational age at birth but differed in upper limits, less than 34 weeks (Collins 2003), and less than or equal to 34 weeks (Marinelli et al. 2001). One study was limited to a gestational age at birth of 32 – 34 weeks (Rocha et al. 2002) and one 32 – 37 weeks (Mosley et al. 2001) and one was limited to preterm infants of birth weight between 1000g and 2500g (Kliethermes et al. 1999). Two trials stratified infants at randomisation, one by birth weight (Rocha et al. 2002) and one by gestational age at birth (Collins 2003).

10.2.1.1.2 Interventions

No Bottle is classified as the treatment and Bottle the control.

Four trials compared bottle feeding with cup feeding (Marinelli et al. 2001; Mosley et al. 2001; Rocha et al. 2002; Collins 2003) and one compared bottle to gavage tube alone (Kliethermes et al. 1999). In all the trials bottle feeds or alternative (cup/tube alone) were

not to replace a breast feed and were only given when the mother could not be present or if extra milk was thought necessary after a breast feed and the infant was assessed to be able to take this orally.

For the cup feeding trials, three followed the cup feeding recommendations of Lang (1994) and Lang et al. (1994), (Marinelli et al. 2001; Rocha et al. 2002; Collins 2003) two used medicine cups, 30 ml (Marinelli et al. 2001) or 60 ml (Collins 2003) and one used the protective cap from a bottle (Rocha et al. 2002). One trial did not state the type of cup used or cup feeding procedure (Mosley et al. 2001). An indwelling nasogastric tube remained in situ for both experimental and control groups in one study (Collins 2003), it is not clear whether this occurred for the remaining trials of cup feeds (Marinelli et al. 2001; Mosley et al. 2001; Rocha et al. 2002)

For the bottle compared to tube alone trial (Kliethermes et al. 1999) all infants were given standard care (including non nutritive breast feeding) until written orders for oral feedings were given. For the control (bottle) group the nasogastric tube was removed as directed by the clinical care team, and all supplementary or complementary feeds were given by bottle. For the experimental group (tube alone) feeds were given by an indwelling 3.5 French Gauge (FG) nasogastric tube (smaller than the commonly used size 5 FG). The tube was removed during the last 24-48 hour parent 'rooming-in' period where a cup or syringe was used if needed.

Skin to skin contact and non nutritive sucking at the breast was encouraged for all infants in two trials (Collins, 2003; Kliethermes, 1999). It is not reported in the trials of Mosley et al. (2001) and Rocha et al. (2002).

Sucking feeds for Bottle and No Bottle groups were commenced according to individual hospital policy. For one trial (Rocha et al. 2002) this was weight based at 1600 grams; for another trial (Marinelli et al. 2001) it was a post menstrual age of greater than or equal to 34 weeks. In a third trial (Collins 2003) sucking feeds commenced when the infants were assessed to be mature enough to coordinate a suck-swallow-breathe-reflex. The remaining two trials did not specify other than when directed by the neonatologist/neonatal nurse practitioner (Kliethermes et al. 1999; Mosley et al. 2001).

Use of a dummy in the included studies varied. Collins (2003) randomised infants to cup/no dummy, cup/dummy, bottle/no dummy, bottle/dummy. There was no statistically significant interaction between no dummy use and cup and therefore results from the marginal groups Cup versus Bottle were able to be analysed independently. A dummy was available during tube feedings for the experimental group in Kliethermes et al. (1999). It is not reported whether a dummy was available outside feeding times in either group. Mosley et al. (2001) does not report whether dummies were used, and in Rocha et al. (2002) a dummy was not used for the experimental (cup) group.

10.2.1.1.3 Outcome measures and results

Not all outcomes were reported in each study.

Only one study (Collins 2003) measured time taken to reach full sucking feeds.

Four studies (Kliethermes et al. 1999; Mosley et al. 2001; Rocha et al. 2002; Collins 2003) measured breast feeding outcomes. Any breast feeding was measured at discharge home from hospital in three trials (Kliethermes et al. 1999; Rocha et al. 2002; Collins 2003), at three months in three trials (Kliethermes et al. 1999; Rocha et al. 2002; Collins 2003), and at six months in two trials (Kliethermes et al. 1999; Collins 2003). Fully breast feeding was measured at discharge home from hospital in three trials (Kliethermes et al. 1999; Mosley et al. 2001; Collins 2003), and at three and six months in one trial (Kliethermes et al. 1999).

Full breast feeding was defined as giving no other solid or liquid apart from vitamin, minerals, juice or ritualistic feedings given infrequently in two trials (Kliethermes et al. 1999; Collins 2003). One trial (Mosley et al. 2001) uses the term 'exclusive' breast feeding but does not define or reference the term. Infants who on discharge home were receiving complementary or supplementary feeds of breast milk were considered as partially breast fed by Kliethermes et al. (1999) and fully breast fed by Collins (2003). Two percent of women (n=6) with 2% of infants (n=7) had chosen to feed their infants expressed breast milk by bottle in Collins (2003). At three and six months post discharge Collins (2003) used the term 'all breast feeds' to represent that the infant's milk feeds were only breast feeds with no other types of milk given, 'partial' meant that the infant's milk feeds were a combination of breast feeds and other types of milk. The intent was to

determine the type of milk feeds infants were receiving (breast or formula) irrespective of whether they were receiving solids. This does not fit with the accepted definition of full breast feeding (Labbok and Krasovec 1990), that is, if an infant is on solids and all milk feeds are breast feeds they are classified as partially breast feeding. The prevalence for 'all breast feeds' cannot therefore be compared to fully breast feeding and is reported in the text and not included in the meta-analysis.

Length of hospitalisation was measured in two trials (Kliethermes et al. 1999; Collins 2003); weight gain in two trials (Rocha et al. 2002; Collins 2003); duration of feeds in two trials (Marinelli et al. 2001; Rocha et al. 2002); cardio-respiratory stability in three trials (Kliethermes et al. 1999; Marinelli et al. 2001; Rocha et al. 2002); and milk aspiration in one trial (Collins, 2003). Health professional or parental satisfaction was not reported in any of the included studies.

10.2.1.2 Excluded studies

Eight studies were excluded (Table 10.1). Five were excluded because the trials only included term infants (Kumar et al. 1989; Schubiger et al. 1997; Howard et al. 1999a; Kramer et al. 2001b; Howard et al. 2003). Rekha et al's (1996) quasi-randomised trial, comparing intermittent nasogastric feeds with feeds given by a paladai during the transition to breast feeds, was excluded as a comparison was not made with bottle feeds. One study was excluded as random or quasi-random allocation to feeding device was unable to be ascertained (Malhotra et al. 1999) and one study was excluded as the end point was transition to full bottle feeds not breast feeds (Poets et al. 1997). Details of the studies of Malhotra et al. (1999) and Poets et al. (1997) are included in the review for the purposes of discussion.

Malhotra et al. (1999)- excluded, unable to verify random or quasi-random allocation.
One hundred infants (normal weight full term n=66, growth restricted term infants n=20 and preterm infants n=14) were studied using a cross-over design comparing feeding by bottle, cup or paladai (traditional Indian cup like feeding device with an open spouted end). Infants were fed by each method at three hour intervals by the same nurse within the same shift. Volume of milk taken, feeding time, spilling and satiety were measured. As this review is concerned with preterm infants, data will only be presented for this group. Compared to the bottle, infants ingested significantly more milk both with the paladai and

the cup, but there was not a significant difference between paladai and cup. Infants took their feeds most rapidly with the paladai (12.8 mls/min, SD 3.6), then cup (4.8 mls/min, SD2.1) then bottle (1.9 mls/min, SD 0.9). No choking or aspiration occurred with the paladai or cup. Spilling was greatest with the cup (36.4% of feed, SD 8.6), the paladai (8.1% of feed, SD 1.6) and least with the bottle (1.7% of feed, SD 2.1). Satiety was defined as the number of hours the baby was settled after a feed, there was a significant difference between bottle (1.7 hours, SD 0.8) and paladai (2.4 hours, SD 0.7). The method of feeding favoured by the nursing staff was unanimously the paladai. The authors report that they no longer use bottles in their nursery.

Poets et al. (1997) - excluded, transition to bottle feeds not breast.

Thirty clinically stable preterm infants (mean gestational age at birth 28.6 weeks, SD 2.1 and mean gestational age at time of study 34 weeks, SD 1.4) were studied using a randomised cross-over design comparing bottle feeding with bolus or slow gavage feeds. Infants were studied when they were on eight feeds per day with approximately half of the feeds given by bottle. Infants were fed by bottle, bolus gavage (over 5 to 10 minutes) and slow gavage (over approximately one hour by pump) in a randomly allocated order at three hour intervals by the same nurse. 30% (n=9) received breast milk and 70% formula. Outcome measurements were undertaken blinded. Continuous heart rate, respiratory rate and oxygen saturation monitoring were performed for a nine hour period. The authors found no significant difference between the feeding methods in overall apnoea or bradycardia frequency. Desaturations ($\leq$ 80%) were significantly more frequent with bottle feeding than either method of gavage; prolonged desaturations ($\geq$ 4 seconds) occurred three times more often with bottle than gavage, and in the two hours following feeds there were significantly more desaturations after bottle feeding. There were no differences in oxygen saturation between bolus and slow gavage feeding methods.

10.2.1.3 Additional information from authors

Additional information was requested from Kliethermes et al. (1999) (breast feeding prevalence, standard deviations for length of hospitalisation and apnoeic/bradycardic episodes, blinding of outcome assessment), Malhotra et al. (1999) (method of study allocation), and Rocha et al. (2002) (prevalence of fully breast feeding at discharge and three months post discharge).

the cup, but there was not a significant difference between paladai and cup. Infants took their feeds most rapidly with the paladai (12.8 mls/min, SD 3.6), then cup (4.8 mls/min, SD2.1) then bottle (1.9 mls/min, SD 0.9). No choking or aspiration occurred with the paladai or cup. Spilling was greatest with the cup (36.4% of feed, SD 8.6), the paladai (8.1% of feed, SD 1.6) and least with the bottle (1.7% of feed, SD 2.1). Satiety was defined as the number of hours the baby was settled after a feed, there was a significant difference between bottle (1.7 hours, SD 0.8) and paladai (2.4 hours, SD 0.7). The method of feeding favoured by the nursing staff was unanimously the paladai. The authors report that they no longer use bottles in their nursery.

Poets et al. (1997) - excluded, transition to bottle feeds not breast.

Thirty clinically stable preterm infants (mean gestational age at birth 28.6 weeks, SD 2.1 and mean gestational age at time of study 34 weeks, SD 1.4) were studied using a randomised cross-over design comparing bottle feeding with bolus or slow gavage feeds. Infants were studied when they were on eight feeds per day with approximately half of the feeds given by bottle. Infants were fed by bottle, bolus gavage (over 5 to 10 minutes) and slow gavage (over approximately one hour by pump) in a randomly allocated order at three hour intervals by the same nurse. 30% (n=9) received breast milk and 70% formula. Outcome measurements were undertaken blinded. Continuous heart rate, respiratory rate and oxygen saturation monitoring were performed for a nine hour period. The authors found no significant difference between the feeding methods in overall apnoea or bradycardia frequency. Desaturations ($\leq$ 80%) were significantly more frequent with bottle feeding than either method of gavage; prolonged desaturations ($\geq$ 4 seconds) occurred three times more often with bottle than gavage, and in the two hours following feeds there were significantly more desaturations after bottle feeding. There were no differences in oxygen saturation between bolus and slow gavage feeding methods.

10.2.1.3 Additional information from authors

Additional information was requested from Kliethermes et al. (1999) (breast feeding prevalence, standard deviations for length of hospitalisation and apnoeic/bradycardic episodes, blinding of outcome assessment), Malhotra et al. (1999) (method of study allocation), and Rocha et al. (2002) (prevalence of fully breast feeding at discharge and three months post discharge).

Additional information was obtained for one of these studies (Kliethermes et al. 1999).

10.2.2 Methodological quality of included studies

Details of the methodological quality of each study are given in the Characteristics of Included Studies (section 10.2.7).

Randomisation: efforts to avoid bias in treatment assignment were adequate in three studies (Kliethermes et al. 1999; Mosley et al. 2001; Collins 2003) and inadequate in two, Marinelli et al. (2001) used coin toss and Rocha et al. (2002) drew lots.

Blinding of treatment: not possible in any study.

Exclusions after randomisation: acceptable, Collins (2003) 5%, Kliethermes et al. (1999) 18%, Mosley et al. (2001) 13%, Rocha et al. (2002) 6%.

Blinding of outcome assessment was not reported in four studies (Kliethermes et al. 1999; Marinelli et al. 2001; Mosley et al. 2001; Rocha et al. 2002) and data for outcomes were collected unblinded in one study (Collins, 2003).

There was a high proportion of non compliance in the trial of Collins (2003). In the experimental group 85/151 (46%) had bottle introduced, and in the control group 1/152 (0.7%) had a cup introduced, an intention to treat analysis was done. Kliethermes et al. (1999) excluded five infants from their analysis because of non compliance. Two infants randomised to the bottle group needed the tube reinserted because of poor tolerance of bottle feeding and three infants randomised to tube alone received bottle feeds. Two infants randomised to cup feeds were excluded from the analysis as a supplementary feed, presumably bottle, had been given in the trial of Mosley et al. (2001). Similarly in the trial of Rocha et al. (2002) one infant, randomised to cup feeds, was excluded from their analysis because a bottle had been introduced.

10.2.3 Results

Due to differences in gestational age range of the included trials subgroup analyses could only be performed for gestational age less than 28 weeks and 28 to less than 37 weeks gestation. Subgroup analyses on type of treatment could be undertaken for Cup versus Bottle and Tube alone versus Bottle.

10.2.3.1 Primary outcomes

As described in section 10.1.3.2 the most appropriate method of analysis for 'time to event' outcomes is survival analysis. There are two such outcomes in this review, time to full sucking feeds and length of hospital stay. Arithmetic mean has been reported for length of hospital stay by Klicthermes et al. (1999). To enable comparisons between studies, the arithmetic mean was used for this review although survivorship mean for Collins (2003) is also reported in the text.

10.2.3.1.1 Time to reach full sucking feeds

In the only study that measured time to reach full sucking feeds (Collins, 2003), infants randomised to bottle feeds reached full sucking feeds significantly earlier than no bottle (cup feeds) (mean difference (MD) 10.37 days, 95% CI 4.65 to 16.09) (Figure 10.10). The survivorship mean was very similar to the arithmetic mean (No Bottle: survivorship mean 53.03 days, SE 2.20, 95% CI 48.73 to 57.34, n=157; arithmetic mean 52.89 days, SD 26.80, range 8 to 118, n=147; Bottle: survivorship mean 42.98 days, SE 1.91, 95% CI 39.25 to 46.71, n=149; arithmetic mean 42.52 days, SD 22.75, range 8 to 112, n=143).

10.2.3.1.2 Subgroup analyses – Time to reach all sucking feeds

Less than 28 weeks gestation – Time to reach all sucking feeds

On subgroup analysis the trend for an increased length of time to reach full sucking feeds for No Bottle now bordered statistical significance for infants less than 28 weeks gestation at birth (Figure 10.11) (MD 7.72 days, 95% CI -0.50 to 15.94). The survivorship mean closely approximated the arithmetic mean (No Bottle: survivorship mean 86.53 days, SE 2.83, 95% CI 80.98 to 92.08, n=39; arithmetic mean 86.53 days, SD 16.76, range 50 to 118, n=34; Bottle: survivorship mean 79.42 days, SE 2.98, 95% CI 73.58 to 85.26, n=30; arithmetic mean 78.81 days, SD 15.58, range 52 to 112, n=26).

28 weeks to less than 37 weeks gestation – Time to reach all sucking feeds

For infants 28 to less than 37 weeks the significant difference remained with No Bottle taking longer to reach full sucking feeds (Figure 10.12) (MD 8.33 days, 95% CI 3.74 to 12.92) (Collins 2003). The survivorship mean closely approximated the arithmetic mean (No Bottle: survivorship mean 42.80 days, SE 1.89, 95% CI 39.15 to 46.50, n=118; arithmetic mean 42.77 days, SD 20.17, range 8 to 108, n=113; Bottle: survivorship mean

34.59 days, SE 1.36, 95% CI 31.92 to 37.26, n=119; arithmetic mean 34.45 days, SD 14.85, range 8 to 87, n=117).

Cup versus Bottle - Time to reach all sucking feeds

In the only trial that measured time to reach all sucking feeds (Collins, 2003) the treatment or intervention was Cup feeds and the control Bottle feeds. This has been presented in section 10.2.3.1.1.

Tube alone versus Bottle – Time to reach all sucking feeds

The trial that compared tube alone to bottle feeds (Kliethermes et al. 1999) did not measure time to reach all sucking feeds.

10.2.3.1.3 Breast feeding – Any

The outcome 'any breast feeding on discharge home' (compared to not breast feeding) was reported for 465 infants in three trials (Kliethermes et al. 1999; Rocha et al. 2002; Collins 2003). One trial showed an increased prevalence of this outcome in the No bottle group (Kliethermes et al. 1999), and two trials (Rocha et al. 2002; Collins 2003) showed a non significant trend towards an increased prevalence in the No Bottle groups. The meta-analysis (Figure 10.13) showed a small but significant increase in the risk of any breast feeding in the No Bottle group (summary RR 1.13, 95% CI 1.01 to 1.2; RD 0.09, 95% CI 0.01 to 0.17; number needed to treat (NNT) 11.1, 95% CI 5.9 to 100). There is, however, a moderate degree of heterogeneity among the trials (Chi^2 =3.42, df=2, P=0.18, I^2=41.6%).

The three trials show the same direction of effect towards an increased prevalence in any breast feeding for No Bottle. The interventions for No Bottle differed, with the trials of Collins (2003) and Rocha et al. (2002) comparing Cup feeds with Bottle feeds and the trial of Kliethermes et al. (1999) Tube alone with Bottle feeds, see sub group analysis '*Cup versus Bottle – Any breast feeding'* and *'Tube alone versus Bottle – Any breast feeding'* (section 10.2.3.1.4) for exploration by intervention.

At three months post discharge the outcome 'any breast feeding' was reported for 444 infants in three trials (Kliethermes et al. 1999; Rocha et al. 2002; Collins 2003). One trial showed an increased prevalence of this outcome in the No bottle group (Kliethermes et al. 1999), and two trials (Rocha et al. 2002; Collins 2003) showed a trend towards an

increased prevalence in the No Bottle groups. The meta-analysis (Figure 10.13) showed a significant increase in the risk of any breast feeding in the No Bottle group (summary RR 1.32, 95% CI 1.06 to 1.64; RD 0.11, 95% CI 0.03 to 0.20; NNT 9.1, 95% CI 5.0 to 33.3).

At six months post discharge the outcome 'any breast feeding' was reported for 364 infants in two trials (Kliethermes et al. 1999; Collins 2003). One trial showed an increased prevalence of this outcome in the No bottle group (Kliethermes et al. 1999), and one trial (Collins 2003) showed a non significant trend towards an increased prevalence in the No Bottle groups. The meta-analysis (Figure 10.13) showed a significant increase in the risk of any breast feeding in the No Bottle group (summary RR 1.50, 95% CI 1.09 to 2.05; RD 0.12, 95% CI 0.03 to 0.21; NNT 8.3, 95% CI 4.8 to 33.3). There is a moderate degree of heterogeneity among the trials (Chi^2 =1.77, df=1, P=0.18, I^2=43.5%). Both trials show the same direction of effect towards an increased prevalence in any breast feeding for No Bottle. As stated previously the interventions for 'No Bottle' differed, with the trial of Collins (2003) comparing Cup feeds with Bottle feeds and the trial of Kliethermes et al. (1999) Tube alone with Bottle feeds.

10.2.3.1.4 Subgroup analyses – Any breast feeding

Less than 28 weeks gestation – Any Breast feeding

Sub group analyses for infants less than 28 weeks gestation at birth were only possible for one trial (Collins 2003) which showed a non significant trend to an increased prevalence of any breast feeding at discharge home (RR 1.70, 95% CI 0.95 to 3.04), and at three months post discharge (RR 1.03, 95% CI 0.39 to 2.73) (Figure 10.14). There was a non significant trend to a decrease in breast feeding prevalence at six months post discharge (RR 0.44, 95% CI 0.12 to 1.61) (Figure 10.14).

28 weeks to less than 37 weeks gestation – Any Breast feeding

Two trials with 314 infants contributed data to the sub group analyses for infants 28 weeks to less than 37 weeks gestation at birth for the outcome 'any breast feeding on discharge home' (Rocha et al. 2002; Collins 2003). Neither trial demonstrated a significant difference between No Bottle and Bottle and the meta-analysis showed no significant difference (summary RR 1.04, 95% CI 0.93 to 1.17) (Figure 10.15). The same two trials with 297 infants were included for the outcome 'any breast feeding at three months post discharge' (Rocha et al. 2002; Collins 2003) and on meta-analysis there was no significant

difference between No Bottle and Bottle groups (summary RR 1.31, 95% CI 0.98 to 1.74) (Figure 10.15). At six months post discharge one trial was included (Collins 2003) with 217 infants and showed no significant difference between the groups (RR 1.02, 95% CI 1.02 to 2.30) (Figure 10.15).

Cup versus Bottle – Any breast feeding

On removing the 'tube alone versus bottle' study of Kliethermes et al. (1999) from the meta-analysis for the outcome 'any breast feeding on discharge home' there is now no heterogeneity ($Chi^2 = 0.21$, df = 1, P = 0.65, $I^2 = 0\%$). The trials of Collins (2003) and Rocha et al. (2002) with 381 infants remained in the meta-analysis. Both trials showed a trend to an increased prevalence of any breast feeding with Cup feeds. The meta-analysis (Figure 10.16) showed a non significant increase in the risk of any breast feeding with Cup feeds (summary RR 1.08, 95% CI 0.96 to 1.22).

At three months post discharge the outcome 'any breast feeding' was reported for 361 infants in two trials (Rocha et al. 2002; Collins 2003). Both trials showed a trend towards an increased prevalence in the Cup groups. The meta-analysis (Figure 10.16) showed a non significant increase in the risk of any breast feeding with Cup feeds (summary RR 1.26, 95% CI 0.95 to 1.67).

At six months post discharge the outcome 'any breast feeding' was reported in only one trial with 281 infants (Collins 2003) which showed an non significant increase in the risk of any breast feeding with Cup feeds (RR 131, 95% CI 0.89 to 1.92) (Figure 10.16).

Tube alone versus Bottle – Any breast feeding

The outcome 'any breast feeding on discharge home' was reported for 84 infants in one trial (Kliethermes et al. 1999) and showed a significant increase in the Tube alone group (RR 1.37, 95% CI 1.08 to 1.74; RD 0.24, 95% CI 0.07 to 0.41; NNT 4.1, 95% CI 2.4 to 14.3) (Figure 10.17).

Any breast feeding at three months post discharge was reported for 83 infants in one trial (Kliethermes et al. 1999) and showed a significant increase with Tube alone (RR 1.69, 95% CI 1.19 to 2.41; RD 0.32, 95% CI 0.13 to 0.52; NNT 3.1, 95% CI 1.9 to 7.7) (Figure 10.17).

Any breast feeding at six months post discharge was reported for 83 infants in one trial (Kliethermes et al. 1999) and showed a significant increase with Tube alone (RR 2.07, 95% CI 1.18 to 3.64; RD 0.29, 95% CI 0.08 to 0.49; NNT 3.5, 95% CI 2.0 to 12.5) (Figure 10.17).

10.2.3.1.5 Fully breast feeding

The outcome 'fully breast feeding on discharge home' (compared to partially and not breast feeding) was reported for 401 infants in three trials (Kliethermes et al. 1999; Mosley et al. 2001; Collins 2003). Two trials showed an increased prevalence of this outcome in the No bottle group (Kliethermes et al. 1999; Collins 2003), and one trial (Mosley et al. 2001) showed a trend towards a decreased prevalence in the No Bottle groups. The meta-analysis (Figure 10.18) showed a significant increase in the risk of fully breast feeding in the No Bottle group (summary RR 1.41, 95% CI 1.19 to 1.69; RD 0.19, 95% CI 0.10 to 0.29; NNT 5.3, 95% CI 3.5 to 10.0).

However, there is a high degree of heterogeneity among trials (chi square=7.01, df=2, P=0.03, I^2=71.5%). The interventions for 'No Bottle' differed with the trials of Collins (2003) and Mosley et al. (2001) comparing Cup feeds with Bottle feeds and the trial of Kliethermes et al. (1999) Tube alone with Bottle feeds. See the sub group analysis *'Cup versus Bottle – Fully breast feeding'* for exploration of effect by intervention (section 10.2.3.1.6).

The outcome 'fully breast feeding at three months post discharge' was reported for 84 infants in one trial (Kliethermes et al. 1999) and showed a significant increase in the No Bottle group (RR 2.31, 95% CI 1.28 to 4.17; RD 0.31, 95% CI 0.11 to 0.51; NNT 3.2, 95% CI 2.0 to 9.1) (Figure 10.18).

At six months post discharge the outcome 'fully breast feeding' was reported for 84 infants in one trial (Kliethermes et al. 1999) and showed a significant increase in the No Bottle group (RR 2.94, 95% CI 1.36 to 6.34; RD 0.30, 95% CI 0.11 to 0.48; NNT 3.3, 95% CI 2.1 to 9.1) (Figure 10.18).

As stated in section 10.1.3.5 the accepted definition for fully breast feeding was unable to be used at three and six months post discharge for the study reported in this thesis. The

term 'all breast feeds' was therefore used to represent that the infant's milk feeds were only breast feeds with no other types of milk given, but it was unknown if solids were being given. The prevalence for 'all breast feeds' cannot therefore be combined with fully breast feeding reported in other studies and are reported in the text and not included in Meta View: (all breast feeds at 3 months post discharge No Bottle n=43/144, 30%; Bottle n=35/139, 25%; all breast feeds at 6 months post discharge No Bottle n=36/142, 25%; Bottle 21/139, 15%).

10.2.3.1.6 Subgroup analyses – Fully breast feeding

Less than 28 weeks gestation – Fully Breast feeding

Data from one trial with 67 infants were able to be included for the outcome 'fully breast feeding on discharge home' for infants less than 28 weeks gestation at birth (Collins 2003). There was no significant difference between No Bottle and Bottle (RR 1.85, 95% CI 0.88 to 3.91) (Figure 10.19).

No studies were able to be included for 'fully breast feeding' at three and six months post discharge for infants less than 28 weeks gestation at birth.

28 weeks to less than 37 weeks gestation – Fully Breast feeding

The outcome 'fully breast feeding on discharge home' for infants 28 to les than 37 weeks at birth was reported for 250 infants in two trials (Mosley et al. 2001; Collins 2003). One trial showed an increased prevalence of this outcome in the No bottle group (Collins 2003), and one trial (Mosley et al. 2001) showed a trend towards a decreased prevalence in the No Bottle groups. The meta-analysis (Figure 10.20) showed a non significant difference in the risk of fully breast feeding in the No Bottle group (summary RR 1.22, 95% CI 1.00 to 1.50; RD 0.12, 95% CI 0.00 to 0.24).

No studies were able to be included for 'fully breast feeding' at three and six months post discharge for infants less 28 to less than 37 weeks gestation at birth.

Cup versus Bottle – Fully breast feeding

On removing the study of Klicthermes et al. (1999) of Tube alone compared to Bottle from the meta-analysis there is now minimal heterogeneity ($Chi^2 = 1.01$, df = 1, P = 0.31, I^2 = 1.0%). Two trials remained for the outcome fully breast feeding on discharge home in the

subgroup Cup versus Bottle (Mosley et al. 2001; Collins 2003). One trial showed a significant increase in the prevalence of fully breast feeding for Cup feeds (Collins, 2003) and the other (Mosley, 2001) a non significant decrease in prevalence. On meta-analysis (Figure 10.21) there was a significant increase in the risk of fully breast feeding (summary RR 1.26, 95% CI 1.03 to 1.54; RD 0.13, 95% CI 0.02 to 0.23; NNT 7.7, 95% CI 4.3 to 50).

No studies were able to be included for the outcome 'fully breast feeding' at three and six months post discharge for Cup versus Bottle.

Tube alone versus Bottle – Fully breast feeding

One trial with 84 infants (Kliethermes et al. 1999) was included for the outcome 'fully breast feeding', for the subgroup Tube alone versus Bottle. There was a significant increase in the risk of fully breast feeding with Tube alone (RR 2.10, 95% CI 1.46 to 3.03; RD 0.46, 95% CI 0.28 to 0.63; NNT 2.2, 95% CI 1.6 to 3.6) (Figure 10.22).

Fully breast feeding at three and six months post discharge for Kliethermes et al. (1999) have been reported in section 10.2.3.1.5.

10.2.3.1.7 Weight gain

Rocha et al. (2002) analysed weight gain one week after beginning oral feeds; in the study reported in this thesis (Collins 2003) weight gain was calculated from birth to discharge home. There were no statistically significant differences in weight gain, reported as grams/kilogram/day, either in the individual trials or in the meta-analysis (371 infants in two trials) (WMD --0.12 g/kg/day, 95% CI - 0.78 to 0.54) (Figure 10.23).

10.2.3.1.8 Subgroup analyses – Weight gain

Less than 28 weeks gestation – Weight gain

Subgroup analysis also did not show any significant difference in weight gain in infants less than 28 weeks gestation. One trial with 63 infants (Collins, 2003) was included in the analysis (MD –0.37 g/kg/day, 95% CI –1.00 to 0.26) (Figure 10.24).

28 weeks to less than 37 weeks gestation – Weight gain

Two trials with 308 infants were included in the meta-analysis for infants 28 to less than 37 weeks (Rocha et al. 2002; Collins 2003) (Figure 10.25). There was no significant

difference in weight gain in either the individual trials or on meta-analysis (WMD - 0.08 g/kg/day, 95% CI –0.89 to 0.72).

Cup versus Bottle - Weight gain

In the two trials that measured weight gain, Cup feeds were compared with Bottle feeds; see section 10.2.3.1.7.

Tube alone versus Bottle – Weight gain

Weight gain was not reported in the only study that compared Tube alone with Bottle feeds (Kliethermes et al. 1999).

10.2.3.1.9 Length of hospitalisation

Length of hospital stay was assessed in two trials with 385 infants (Kliethermes et al. 1999; Collins 2003). The study reported in this thesis showed a significantly increased length of hospital stay of 10 days with No Bottle (Collins 2003) and the remaining trial a non significant trend towards an increased length of stay of 1.6 days with No Bottle (Kliethermes et al. 1999). There was a significant increase in length of stay in the meta-analysis (WMD 6.63 days, 95% CI 1.85 to 11.41) (Figure 10.26).

However, there was moderate heterogeneity among trials (chi square=2.92, df=1, P=0.09, I^2=65.8%). The intervention for 'No bottle' differed between the two trials with Collins (2003) using Cup and Kliethermes Tube alone. Caution needs to be used in interpreting the meta-analysis due to the moderate degree of heterogeneity. It is possible that there are real differences in the effect on length of stay between the two 'No bottle' interventions, cup and tube alone, and therefore a meta-analysis is not appropriate.

In the trial of Kliethermes et al. (1999) the length of stay for those in the No Bottle (tube alone) group was nearly 28 days less than for the study reported in this thesis (Collins 2003) and 19 days less for those in the Bottle group. The infants in Kliethermes et al. (1999) study were more mature, an inclusion criterion was preterm infants with birth weight 1000g to 2500g. Their study sample consisted of gestational age at birth: 32 weeks, SD not reported, range 26-35 weeks for tube alone; and 32 weeks, SD not reported, range 28–35 weeks for bottle. An inclusion criterion for the study reported in this thesis (Collins 2003) was infants less than 34 weeks gestation and the study sample consisted of

gestational age at birth: 29.4 weeks, SD 2.6, range 23-33 for cup; and 30.0 weeks, SD 2.5, range 24-33 for bottle. This difference in maturity may explain some of the differences in length of stay seen between the studies.

For the study reported in this thesis (Collins, 2003) the survivorship mean closely approximated the arithmetic mean (No bottle 62.66 days, SE 2.47, 95% CI 57.81 to 67.51, n=161; arithmetic mean 62.17 days, SD 30.37, range 15 to 148, n=149; Bottle: survivorship mean 53.45 days, SE 2.21, 95% CI 49.11 to 57.79, n=158; arithmetic mean 52.09 days, SD 24.15, range 12 to 119, n=152).

10.2.3.1.10 Subgroup analyses – Length of hospitalisation

Less than 28 weeks gestation – length of hospitalisation

On subgroup analysis one trial, with 65 infants, contributed data for gestational age at birth less than 28 weeks (Collins 2003) and showed a significant increase in length of stay (Figure 10.27) for No Bottle (MD 9.96 days, 95% CI 1.61 to 18.31). The survivorship mean closely approximated the arithmetic mean (No Bottle: survivorship mean 98.38 days, SE 2.92, 95% CI 92.65 to 104.16, n=42; arithmetic mean 98.29 days, SD 17.63, range 70 to 131, n=35; Bottle: survivorship mean 88.62 days, SE 2.95, 95% CI 82.83 to 94.41, n=34; arithmetic mean 88.33 days, SD 16.69, range 59 to 119, n=30).

28 weeks to less than 37 weeks gestation – length of hospitalisation

For the subgroup analysis gestational age at birth 28 weeks to less than 37, one trial contributed data from 236 infants (Collins, 2003), and showed a significant increase in length of stay (Figure 10.28) for No Bottle (MD 7.90 days, 95% CI 2.63 to 13.17). The survivorship mean closely approximated the arithmetic mean (No Bottle: survivorship mean 51.10 days, SE 2.26, 95% CI 46.67 to 55.52, n=119; arithmetic mean 51.08 days, SD 24.22, range 15 to 148, n=114; Bottle: survivorship mean 44.54 days, SE 1.975, 95% CI 40.68 to 48.39, n=124; arithmetic mean 43.18 days, SD 15.97, range 12 to 109, n=122).

Cup versus Bottle - length of hospitalisation

The study reported in this thesis was the only trial of Cup versus Bottle to measure length of hospital stay (Figure 10.29). There was a significant increase in length of hospital stay with Cup feeds (MD 10.08 days, 95% CI 3.87 to 16.29).

Tube alone versus Bottle – length of hospitalisation

Kliethermes et al. (1999) was the only trial of Tube alone versus Bottle and showed no significant difference in length of hospital stay (Figure 10.30) (MD 1.60 days, 95% CI -5.89 to 9.09).

10.2.3.1.11 Duration of feed

The time taken for a feed was reported for 190 infants in two trials (Marinelli et al. 2001; Rocha et al. 2002) and differed between the trials. In the Marinelli et al. (2001) trial there was a non significant difference with No Bottle slower (MD 3.80 minutes, 95% CI –12.01 to 19.61). In the Rocha et al. (2002) trial bottle feeds took longer than No Bottle (MD -1.60 minutes, 95% CI -3.69 to 0.49). On meta-analysis there was no statistically significant difference in duration of feed (WMD 1.51 minutes, 95% CI –0.57 to 3.58) (Figure 10.31).

10.2.3.1.12 Sub group analyses – Duration of feed

Less than 28 weeks gestation – duration of feed

No trials were able to be included for this outcome.

28 weeks to less than 37 weeks gestation – duration of feed

Subgroup analysis was able to be performed for gestation 28 weeks to less than 37 weeks (78 infants, one trial) (Rocha et al. 2002) with no statistically significant difference in duration of feed (MD -1.60 minutes, 95% CI -3.69 to 0.49) (Figure 10.32).

Cup versus Bottle – duration of feed

The two trials that measured duration of feed had as their treatment group Cup feeds versus Bottle feeds as the control. These results are presented in section 10.2.3.1.11.

Tube alone versus Bottle – duration of feed

The only trial that compared Tube alone to Bottle feeds did not measure duration of feed (Kliethermes et al. 1999).

10.2.3.1.13 Cardio-respiratory stability

The number of episodes of apnoea or bradycardia per infant were reported in two trials (Kliethermes et al. 1999; Marinelli et al. 2001) but due to differences in reporting a meta-analysis was unable to be performed. Kliethermes et al. (1999) reported significantly fewer apnoeic and bradycardic incidents for No Bottle (tube alone) (mean 127 incidents, SD 197, n=46) compared to Bottle (mean 136 episodes, SD 141, n=38; P=0.0006). The No Bottle (tube alone) infants however, had significantly more episodes that required stimulation (mean 32.7 episodes, SD 68.1, n=38 versus 23.3 episodes, SD 57, n=46; P=0.0001). The apnoeic and bradycardic episodes were measured over the entire hospital stay, not just those associated with feeding. Marinelli et al. (2001) reported episodes of apnoea or bradycardia per infant (Bottle: mean 0.36, SD 6.14, n=56; No Bottle: 0.16, SD 3.44, n=56; P=0.11) and as a percent of feedings (Bottle 22%, No Bottle 13%, P=0.23) with no statistically significant difference between the two methods of feeding. The apnoeic and bradycardic episodes were measured ten minutes before the feeding and for the duration of the feed.

Heart rate and respiratory rate were reported in one cross-over trial (Marinelli et al. 2001) (56 infants). There was a non significant clinical and statistical trend to a higher heart rate with bottle feeds (Figure 10.33) (MD -3.40, 95% CI –7.47 to 0.67) and no significant difference in respiratory rate (MD -0.90, 95% CI –3.47 to 1.67) (Figure 10.34).

Two trials reported mean oxygen saturation during feeds but due to differences in reporting a meta-analysis was unable to be performed (Marinelli et al. 2001; Rocha et al. 2002). Marinelli et al. (2001) reported a statistically significant difference in mean oxygen saturation during feeds (Bottle: mean 94.5, SD 5.3, n=56; No Bottle: 96.5, SD 2.6, n=56; P=0.02), the lower end of the range for bottle feeds was 74.4% compared to 90% for No bottle (cup) feeds. Rocha et al. (2002) reported no significant difference in the mean of the lowest oxygen saturation during feeds (Bottle: mean 87.7, SD 7.6, range 68-97; No Bottle (cup): mean 90.8, SD 4.8, range 75-99).

Two trials reported oxygen desaturations during feeds (Marinelli et al. 2001; Rocha et al. 2002). A meta-analysis was unable to be performed due to the differences in reporting. Marinelli et al. (2001) reported the fraction of oxygen desaturations less than 90%, calculated as the number less than 90% per total number of oxygen saturation measurements, they reported statistically significantly less desaturations (P=0.02) with No

Bottle (cup) feeds (mean 0.05, SD 0.09, n=56) compared to Bottle feeds (mean 0.13, SD 0.22, n=56). Rocha et al. (2002) reported a non statistically significant trend to more desaturations less than 90% in infants bottle fed (19/34, 55.9%) compared to No Bottle (cup) (18/44, 40.9%). However they reported a statistically significant difference in the proportion of desaturations less than 85% with more occurring in those bottle fed (12/34, 35.3%) than No Bottle (cup) fed (6/44, 13.6%, P=0.02).

10.2.3.1.14 *Subgroup analyses – cardio respiratory stability*

Less than 28 weeks gestation – cardio respiratory stability

No trials were able to be included for this subgroup.

28 weeks to less than 37 weeks gestation – cardio respiratory stability

No trials were able to be included for this subgroup.

Cup versus Bottle - cardio respiratory stability

The only included trial that measured apnoea and bradycardia, heart rate and respiratory rate in Cup versus Bottle (Marinelli, 2001) has been discussed in section 10.2.3.1.13. The two trials (Marinelli et al. 2001; Rocha et al. 2002) that measured oxygen saturation in their trials comparing Cup versus Bottle has been discussed in section 10.2.3.1.13.

Tube alone versus Bottle - cardio respiratory stability

The only included trial of Tube alone versus Bottle measured episodes of apnoea and bradycardia (Kliethermes et al. 1999), this has been discussed in section 10.2.3.1.13.

10.2.3.1.15 Milk aspiration – on radiologic assessment

Milk aspiration was not reported in any of the studies (535 infants in five trials).

10.2.3.2 Secondary outcomes:

10.2.3.2.1 Satisfaction

Parental or health professional satisfaction was not reported in any of the trials.

10.2.3.3 A posteriori outcomes

Two important outcomes, episodes of choking and volume of feed taken, have been reported in one of the trials (Marinelli et al. 2001), these outcomes were not included in the objectives for this review. There were no statistically significant differences between episodes of choking per infant for Bottle feeds (mean 0.65, SD 7.48) compared to No Bottle (cup) feeds (mean 0.65, SD 7.48). The volume of feed taken differed significantly with bottle fed infants having a higher intake per feed (mean 27.2 mls, SD 87.56) than no bottle (cup) fed infants (mean 20.9, SD 84.56, P=0.001) (Marinelli et al. 2001). When expressed as volume of feed taken/volume prescribed infants bottle fed took 15% more of their prescribed volume (mean 0.76, SD 2.25) than no bottle (cup) fed infants (mean 0.61, SD 2.25; P=0.003).

10.2.4 Discussion

In this review, the search revealed six trials that met pre-specified eligibility criteria and one other that may do so but information was unavailable from the author.

10.2.4.1 Limitations of the review

The quality of the studies was variable with three of the five included attempting to conceal the randomisation process. Ascertainment of outcomes was generally complete. An intention to treat analysis was not undertaken in three of the studies.

10.2.4.2 Feeding and growth outcomes

Providing supplementary or complementary feeds by bottle during the transition to breast feeds significantly shortened the time taken to reach all sucking feeds in the only study that measured this outcome (Collins, 2003). On subgroup analysis there was no significant difference found for infants less than 28 weeks gestation (Collins, 2003).

On meta-analysis, breast feeding (any) on discharge home and at three and six months post discharge was significantly increased if a bottle was not used during the transition to breast feeds (Kliethermes et al. 1999; Rocha et al. 2002; Collins 2003). In the subgroup analysis by intervention, use of a cup neared but did not reach significance at the same time points (Rocha et al. 2002; Collins 2003), and tube alone was statistically significant at all the time points (Kliethermes, 1999).

There was a significant benefit in not using a bottle on infants fully breast feeding on discharge home (Kliethermes et al. 1999; Mosley et al. 2001; Collins 2003). The significant effect remained for cup versus bottle (Mosley et al. 2001; Collins 2003), but was dominated by the trial of Collins (2003). The significant effect remained for tube alone versus bottle (Kliethermes et al. 1999).
Thee were no reports of infants being dissatisfied with tube alone or cup in four of the included studies (Kliethermes et al. 1999; Marinelli et al. 2001; Mosley et al. 2001; Rocha et al. 2002). In the study reported in this thesis (Collins, 2003) some parents reported that their infants were not satisfied with cup feeds and introduced a bottle because of this.

The method of feeding did not affect weight gain (Rocha et al. 2002; Collins 2003).

A meta-analysis for length of hospital stay was not appropriate due to moderate heterogeneity between the two trials that measured this outcome (Kliethermes et al. 1999; Collins 2003). In the trial comparing tube alone to bottle feeds, (Kliethermes et al. 1999) no significant difference was found in length of hospital stay. In contrast there was a mean increase of 10 days for infants cup fed compared to bottle fed in the study reported in this thesis (Collins, 2003).

There was conflicting evidence for the duration of feeds. When comparing bottle with cup, one trial reported that infants took less time to feed by bottle (Marinelli et al. 2001) and in one trial the infants took less time to feed by cup (Rocha et al. 2002); on meta-analysis there was no statistically significant difference in duration of feeds. An identified study not included in this review (Malhotra et al. 1999) reported paladai as being the quickest, then cup, and bottle the slowest.

There may have been differing feeding management practices among the studies, which require verification from the authors. For example in the trial of Kliethermes et al. (1999), two infants randomised to the bottle group were excluded from their analysis because they did not manage bottle feeds and required a tube to be re-inserted. In the trial of Collins (2003) infants randomised to bottle feed who were unable to complete a bottle feed (when the mother was unable to be present for a breast feed) were fed the remainder of their milk quota by tube.

10.2.4.3 Safety outcomes

Infants are more unstable when bottle fed than cup or tube fed. An increased frequency of oxygen desaturations occurred with bottle feeds compared to cup feeds (Marinelli et al. 2001; Rocha et al. 2002). An identified study not included in this review (Poets et al. 1997) also reported an increased frequency of desaturations with bottle feeds compared to tube alone. The prevalence of apnoeic and bradycardic episodes were similar between cup and bottle (Marinelli et al. 2001). There was a reduced frequency of apnoeic and bradycardic episodes with tube alone compared to bottle (Kliethermes et al. 1999), in contrast, an identified study not included in this review (Poets et al. 1997) reported no significant difference between tube and bottle.

No studies reported milk aspiration with either method, episodes of choking were similar between bottle and cup feeds (Marinelli et al. 2001). An identified study not included in this review (Malhotra et al. 1999) reports no episodes of choking with cup or paladai.

Marinelli et al. (2001) reports an increased volume of feed taken with bottle compared to cup. In contrast an identified study not included in this review (Malhotra et al. 1999) reported that infants ingested significantly more milk, both with the paladai and the cup, compared to bottle, but no significant difference between paladai and cup.

10.2.4.4 Satisfaction

None of the studies measured parental satisfaction. One identified study not included in this review (Malhotra et al. 1999) reports that the nurses all preferred the paladai because of the ease of cleaning and sterilisation, ease of training mothers and less time involved in feeding.

10.2.5 Reviewer's conclusions

Implications for practice

Not using a bottle in the preterm infant's transition to breast feeds has significant advantages for breast feeding outcomes and cardio respiratory stability. The method of 'no bottle' is less clear. Tube alone compared to bottle significantly increased 'any' and 'fully' breast feeding with no effect on length of hospital stay. However, cup feeding compared to bottle neared significance for an increased prevalence of 'any' breast feeding, significantly increased the prevalence of 'fully' breast feeding but also significantly

increased the time taken to reach all sucking feeds and the length of hospital stay. Some infants were not satisfied with cup feeds in one trial (Collins 2003) but no reports of dissatisfaction were made in the other included studies. Compliance for a tube alone strategy was high (Kliethermes et al. 1999) but variable for cup feeding with high compliance in the trial of Rocha et al. (2002) and Mosley et al. (2001) and poor compliance in the trial of Collins (2003).

There do not appear to be any negative effects of a tube alone approach in the transition to breast feeds, but a non significant increase in any breast feeding and a longer duration of time to full sucking feeds and length of stay with cup feeds.

Implications for research

There is a need for further trials in other centres to investigate the ideal method of a No Bottle approach in the transition to breast feeds for preterm infants. Such trials should have concealed random allocation, complete follow-up of all randomised infants, and adequate sample size to evaluate length of hospital stay, weight gain, breast feeding prevalence (any and fully) on discharge home and at three and six months post discharge; and parental and staff satisfaction with feeding method. There is a need to repeat the 'tube alone' trial in other centres and the cup feeding trial given the conflicting compliance rates among the included trials.

10.2.6 Potential conflict of interest

The reviewer is author of an included trial

10.2.7 Characteristics of included studies

Study	**Collins (2003)**
Methods	Randomised, factorial, stratified by gestational age at birth <28 weeks and 28 - <34 weeks. Study duration – 3 years Blinding of randomisation – yes Blinding of intervention – no, not possible Complete follow up – 16 post randomisation exclusions: 12 infants died, 4 withdrawals Blinding of outcome measurement and analysis – no

Participants	Two tertiary centres, Australia Inclusion criteria: gestational age at birth < 34 weeks (Experimental: mean 29.4 weeks, SD 2.6, range 23-33; Control: mean 30.0 weeks, SD 2.5, range 24-33), mother wishes to breast feed, had not been fed by cup or bottle, no congenital abnormality precluding sucking feeds, dummy use ≤48 hours. Sample size 319 randomised, 303 included in analysis. Number randomised to each group = 151 (experimental/cup), 152 (control/bottle).
Interventions	Both groups infants breast fed when mother present. If prescribed volume not taken by cup/bottle then given via indwelling nasogastric tube. Randomised to cup/no dummy, cup/dummy, bottle/no dummy, bottle/dummy. Experimental: supplementary and complementary feeds given by cup according to Lang's (1994) recommendations. 60 ml medicine cup used. Control: supplementary and complementary feeds given by bottle
Outcomes	Breast feeding prevalence any and fully at discharge, and 'all' and any at 3 and 6 months Days to all sucking feeds Length of hospitalisation Weight gain
Notes	Power calculation done Intention to treat analysis undertaken, (high proportion of non compliance: experimental group 85/151 (46%) had bottle introduced, control group 1/152 (0.7%) had a cup introduced)
Allocation concealment	A

Study	**Kliethermes et al. (1999)**
Methods	Randomised Study duration – 22 months Blinding of randomisation – yes Blinding of intervention – no, not possible Complete follow up – 15 excluded post randomisation: 1 necrotising enterocolitis, 1 subglottic stenosis, 2 transfer to another hospital, 5 non compliance with study protocol, 1 maternal scleroderma, 2 maternal cocaine use, 1 neonatal death, 1 oxygen requirement >40% at 1 month of age, 1 congenital heart defect. Blinding of outcome measurement and analysis – can't tell

Participants	Single centre, Tertiary perinatal centre, United States of America Inclusion criteria: birth weight 1000g – 2500g, less than one week of age, no congenital or neurological abnormalities that interfered with cardiopulmonary status. Gestational age at birth: 32 weeks, SD not reported, range 26-35 weeks (experimental); 32 weeks, SD not reported, range 28–35 weeks (control); birth weight 1.73kg, range 1.05kg-2.43kg (experimental), 1.64kg, range 1.0kg–2.35kg (control), twins 8 (21%) experimental, 16 (35%) control. Sample size 99 randomised, 84 included in analysis. Number randomised to each group = 38(Experimental/tube alone), 46 (Control/bottle)
Interventions	Both groups infants breast fed when mother present. Experimental group: Feeds given by indwelling size 3.5 FG nasogastric tube when mother not available or complement after breast feed required. Tube removed during last 24-48 hour parent 'rooming-in' period, a cup or syringe used during this time if needed. Control group: Fed by bottle when mother not available or complement after breast feed required. Nasogastric tube removed.
Outcomes	Breast feeding duration Apnoea/bradycardia Length of hospitalisation
Notes	No power calculation
Allocation concealment	A
Study	**Marinelli et al. (2001)**
Methods	Randomised cross-over trial Study duration – 22 months Blinding of randomisation – no, coin toss Blinding of intervention – no, not possible for patient or provider Complete follow up - yes Blinding of outcome measurement and analysis – can't tell
Participants	Single centre, NICU, United States of America ≤34 weeks gestation at birth (Mean 30.4 weeks, SD 2.4), mother wishes to breast feed, infant not requiring oxygen. Randomised when ready for oral feeds other than breast (Mean 34.3 weeks, SD 0.5) Sample size = 56

Interventions	Randomised to one cup feed then one bottle, or one bottle feed then one cup, washout period minimum of one gavage feed. Experimental group: Fed by cup (30 ml medicine cup) according to Lang's (1994) recommendations Control group: Fed by bottle with standard yellow teat.
Outcomes	Duration of feeds Cardio-respiratory stability (heart rate, respiratory rate, oxygen saturation, apnoea, bradycardia) Volume of feed taken, choking, vomiting, spitting
Notes	Intention to treat analysis, power calculation done
Allocation concealment	C
Study	**Mosley et al. (2001)**
Methods	Randomised, pilot study Study duration – 3 months Blinding of randomisation – yes Blinding of intervention – no, not possible Complete follow up – 2 excluded post randomisation: had been given a supplementary feed Blinding of outcome measurement and analysis – can't tell
Participants	Single centre, Special Care Baby Unit, District General Hospital, England Inclusion criteria: gestational age at birth 32-37 weeks, mother wishes to breast feed, no congenital abnormality, no maternal preference for cup or bottle, had not been fed by cup or bottle. Sample size 16 randomised, 14 included in analysis. Number randomised to each group = 6 (experimental/cup), 8 (control/bottle)
Interventions	Experimental: supplementary feeds given by cup Control: supplementary feeds given by bottle
Outcomes	Exclusive breast feeding prevalence on discharge home
Notes	
Allocation concealment	A

Study	**Rocha et al. (2002)**
Methods	Randomised, stratified by weight (500 – 999g, 1000-1499g, 1500-1699g) Study duration – 18 months Blinding of randomisation - no, drawing of lots Blinding of intervention - no, not possible Complete follow up – 5 excluded post randomisation: 1 gastro-oesophageal reflux, 1 severe bronchopulmonary dysplasia, 1 maternal cocaine use, 2 non compliance with cup feeding and bronchopulmonary dysplasia. Blinding of outcome measurement and analysis – can't tell
Participants	Single Centre, NICU, University Hospital, Brazil Inclusion criteria: gestational age at birth 32-34 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 1276g, SD 283g; control: mean 1262g, SD 270g), mothers wished to breast feed, clinically stable, not initially on parenteral nutrition. Sample size 83 randomised, 78 included in analysis. Number randomised to each group = 44(experimental/cup), 34 (control/bottle)
Interventions	Infants in both groups fed by orogastric tube until 1600g. Experimental: supplements or complements given by cup according to the recommendations of Kuehl (1997) and Lang (1994). Not offered a dummy Control: supplements or complements given by bottle.
Outcomes	Breast feeding prevalence on discharge, first follow up visit and 3 months post discharge Weight gain (one week after beginning oral feeds) Length of feeding time (one week after beginning oral feeds)
Notes	No power calculation
Allocation concealment	C

10.2.8 Characteristics of excluded studies

The characteristics of the excluded studies are detailed in Table 10.1.

Table 10.1 Characteristics of excluded studies

Study	Reason for exclusion
Howard et al. (1999a)	Term infants
Howard et al. (2003)	Term infants
Kramer et al. (2001b)	Term infants
Kumar et al. (1989)	Infants less than six months of age on artificial milk.
Malhotra et al. (1999)	Unable to verify random or quasi-random allocation.
Poets et al. (1997)	Transition to full bottle feeds not breast, includes infants receiving breast milk and infants receiving formula
Rekha et al. (1996)	Compared tube alone to paladai.
Schubiger et al. (1997)	Term infants

10.2.9 MetaView Graphs

Figure 10.10 Days to all sucking feeds, No Bottle versus Bottle

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (all trials)
Outcome: Days to full sucking feeds

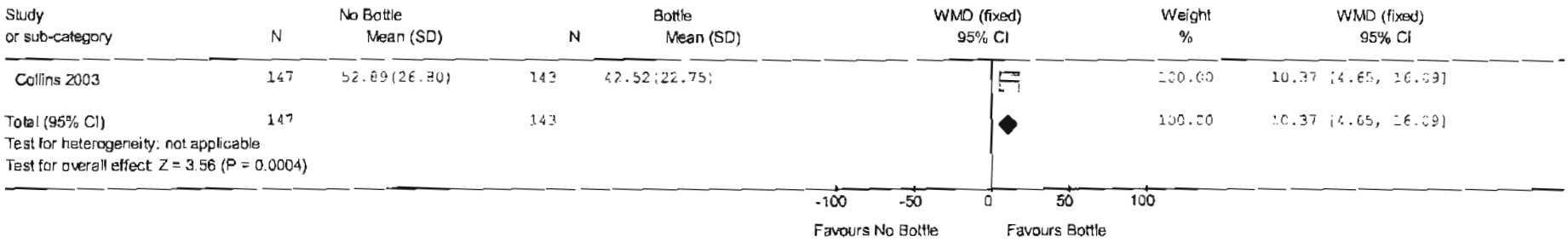


Figure 10.11 Days to all sucking feeds, bottle versus no bottle, <28 weeks gestation

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (<28 weeks)
Outcome: Days to full sucking feeds

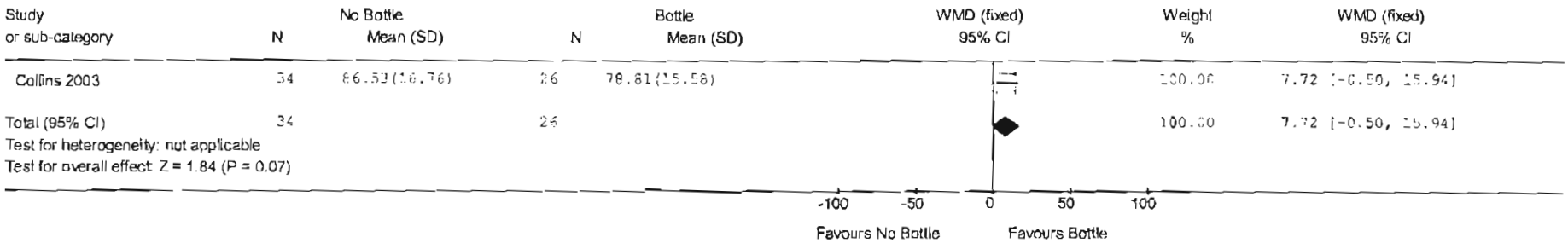


Figure 10.12 Days to all sucking feeds, bottle versus no bottle, 28 to < 37 weeks gestation

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (28 to <37 weeks)
Outcome: Days to full sucking feeds

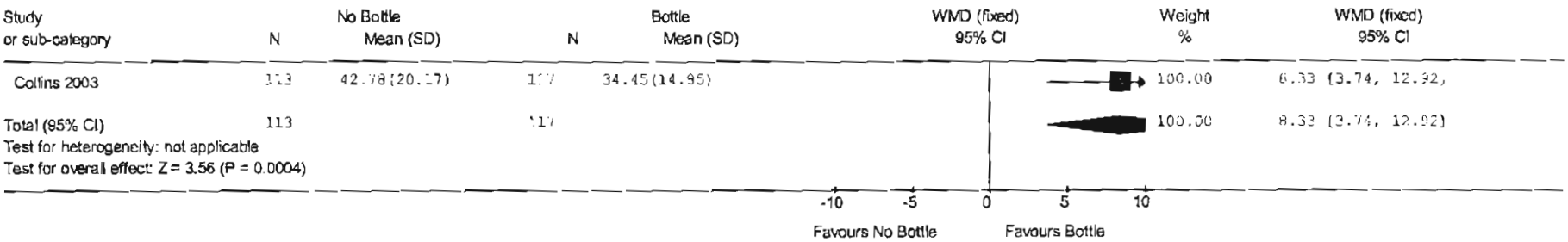


Figure 10.13 Any breast feeding, No Bottle versus Bottle

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (all trials)
Outcome: Any breast feeding

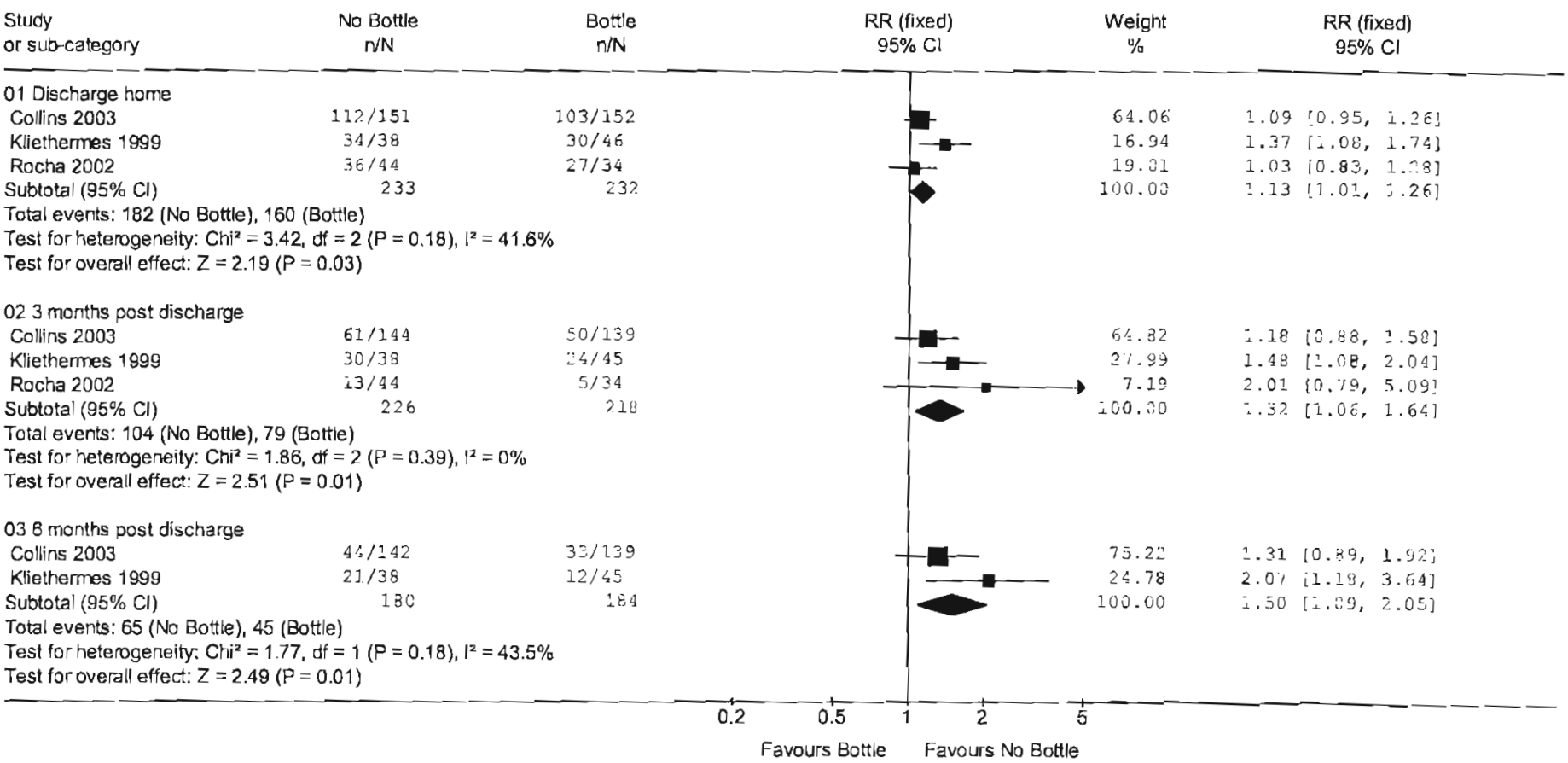


Figure 10.14 Any breast feeding, No Bottle versus Bottle, <28 weeks gestation

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (<28 weeks)
Outcome: Any breast feeding

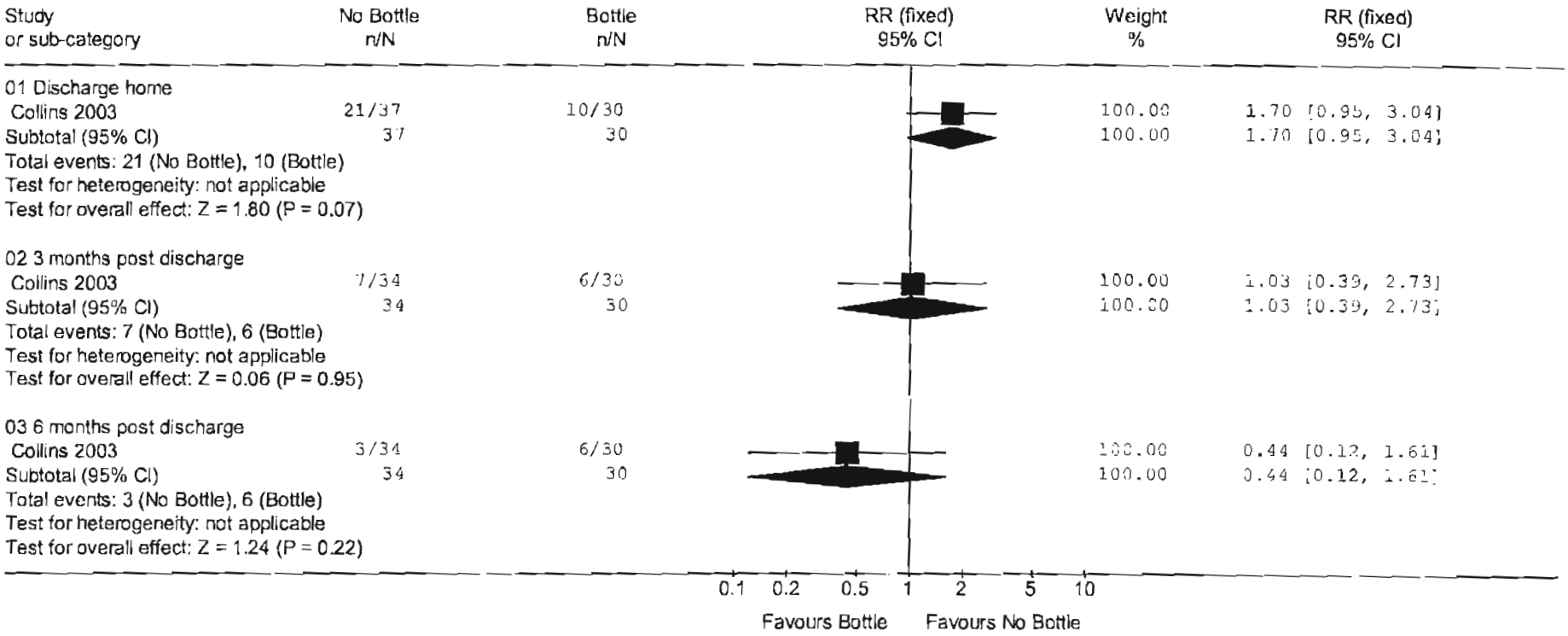


Figure 10.15 Any breast feeding, No Bottle versus Bottle, 28 to <37 weeks gestation

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (28 to <37 weeks)
Outcome: Any breast feeding

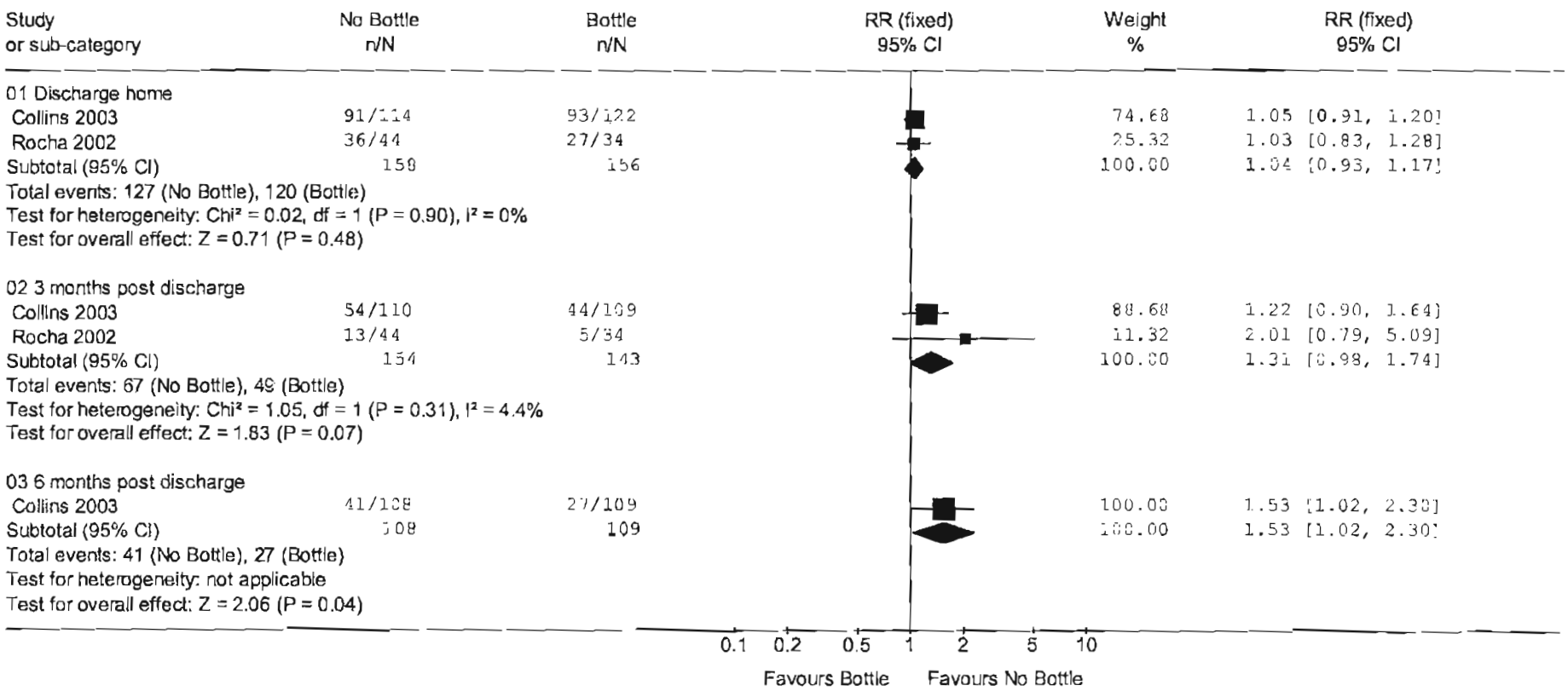


Figure 10.16 Any breast feeding, Cup versus Bottle

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: Cup versus Bottle
Outcome: Any breast feeding

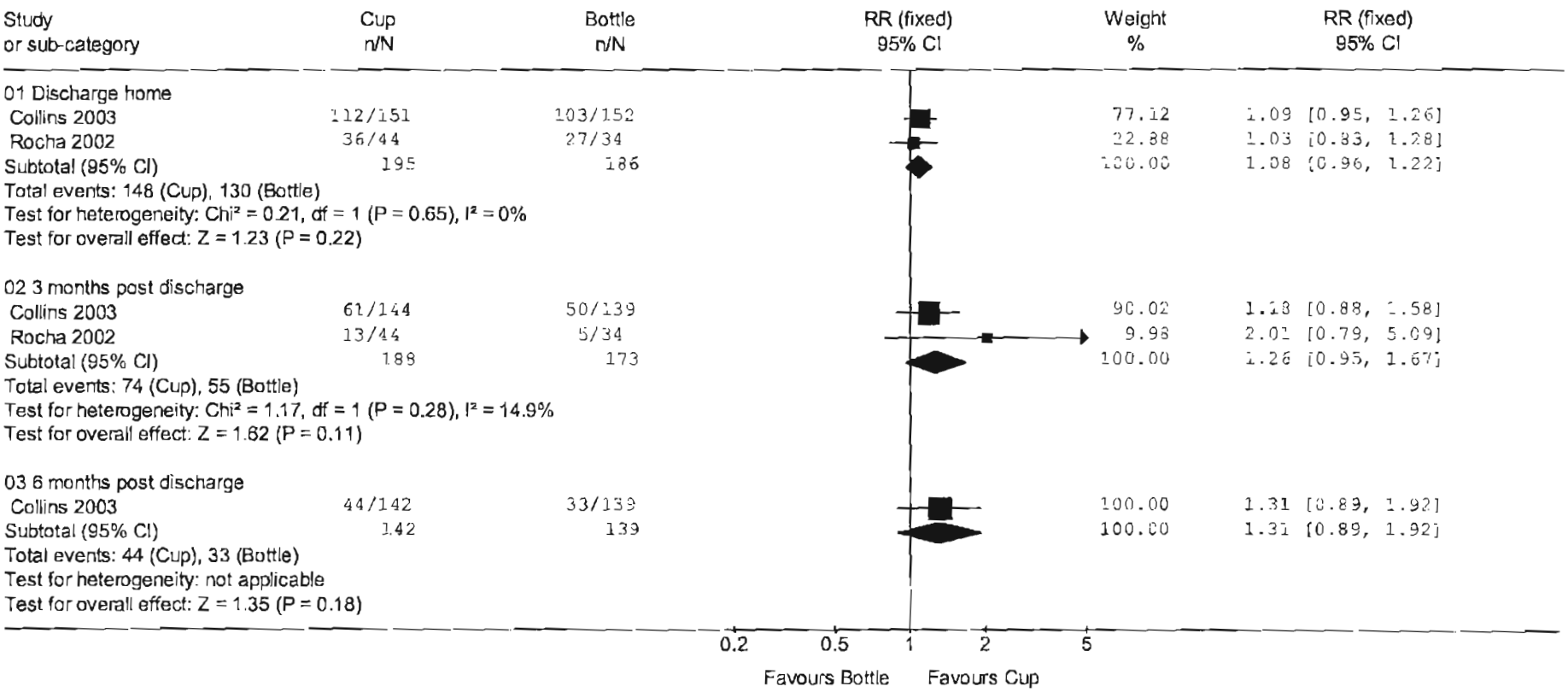


Figure 10.17 Any breast feeding, Tube alone versus Bottle

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: Tube alone versus Bottle
Outcome: Any breast feeding

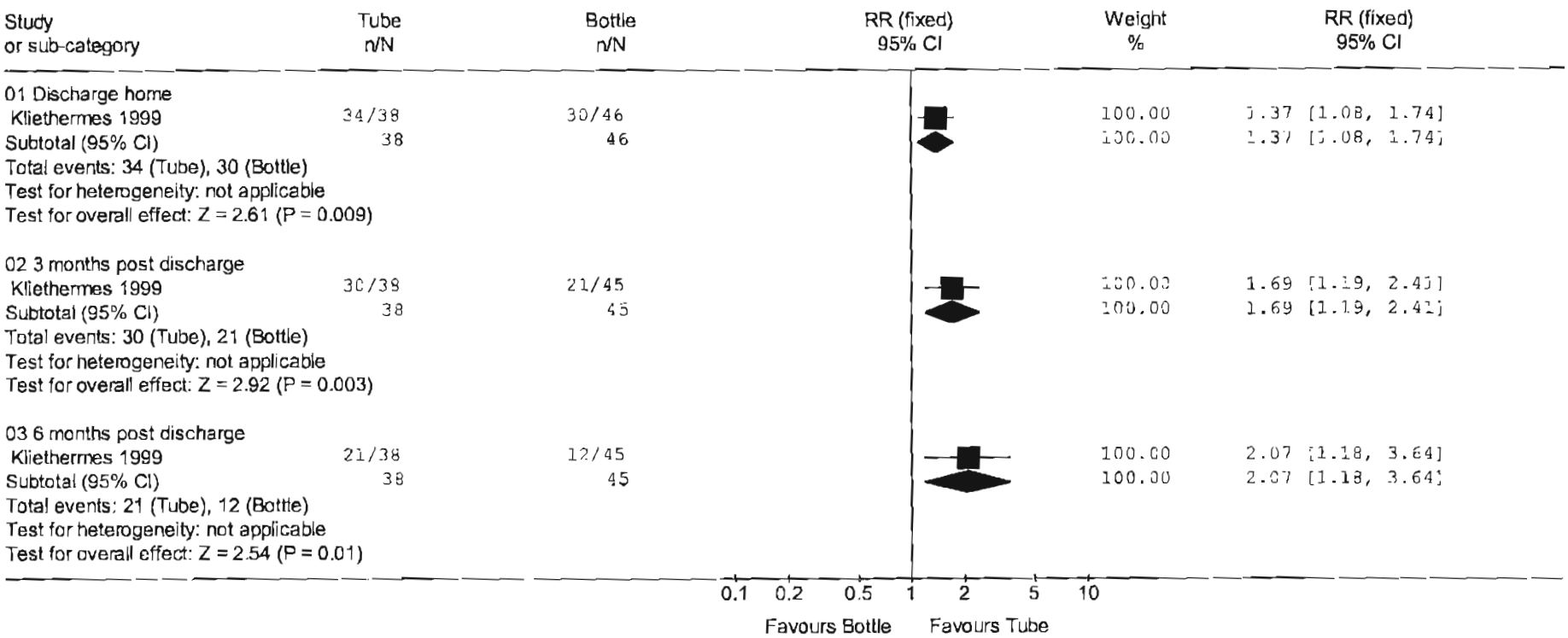


Figure 10.18 Fully breast feeding, No Bottle versus Bottle

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (all trials)
Outcome: Fully breast feeding

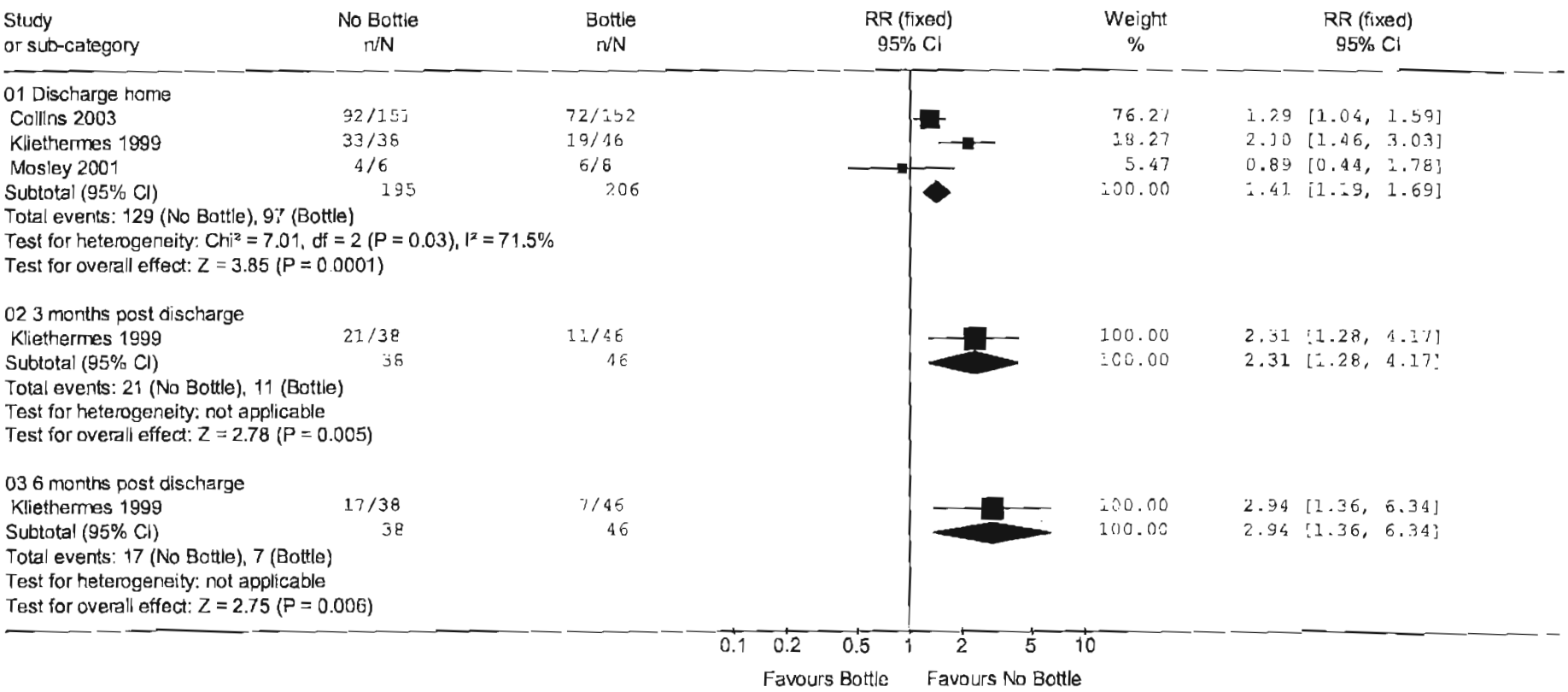


Figure 10.19 Fully breast feeding, No Bottle versus Bottle, <28 weeks gestation

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (<28 weeks)
Outcome: Fully breast feeding on discharge home

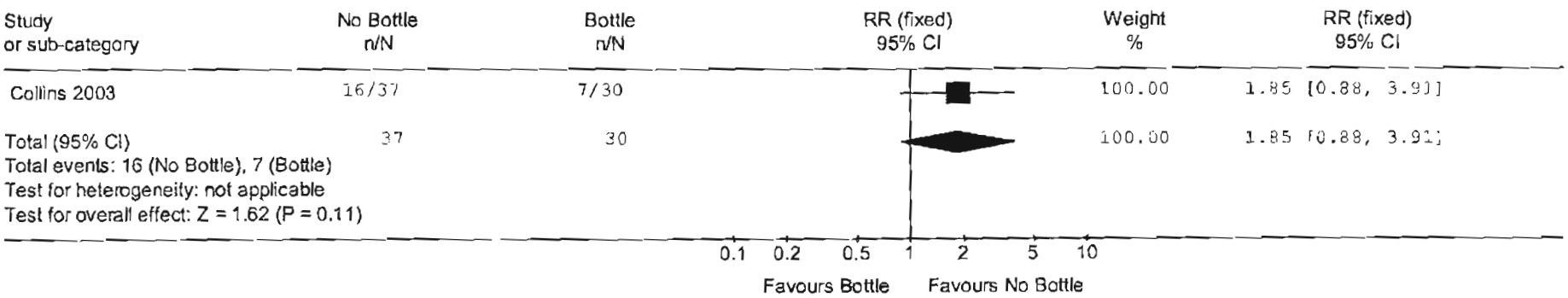


Figure 10.20 Fully breast feeding, No Bottle versus Bottle, 28 to <37 weeks gestation

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (28 to <37 weeks)
Outcome: Fully breast feeding on discharge home

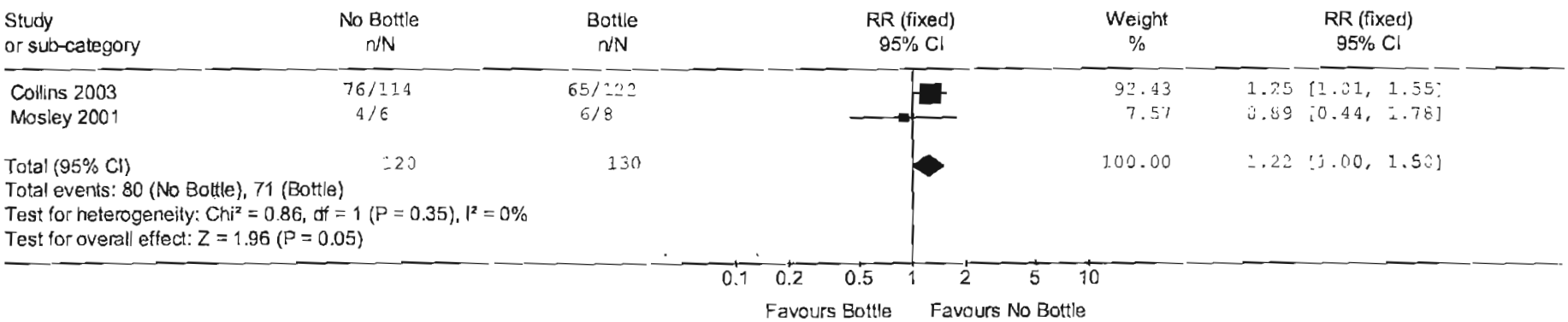


Figure 10.21 Fully breast feeding, Cup versus Bottle

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants. (29August03)
Comparison: 04 Cup versus Bottle
Outcome: 02 Fully breast feeding on discharge home

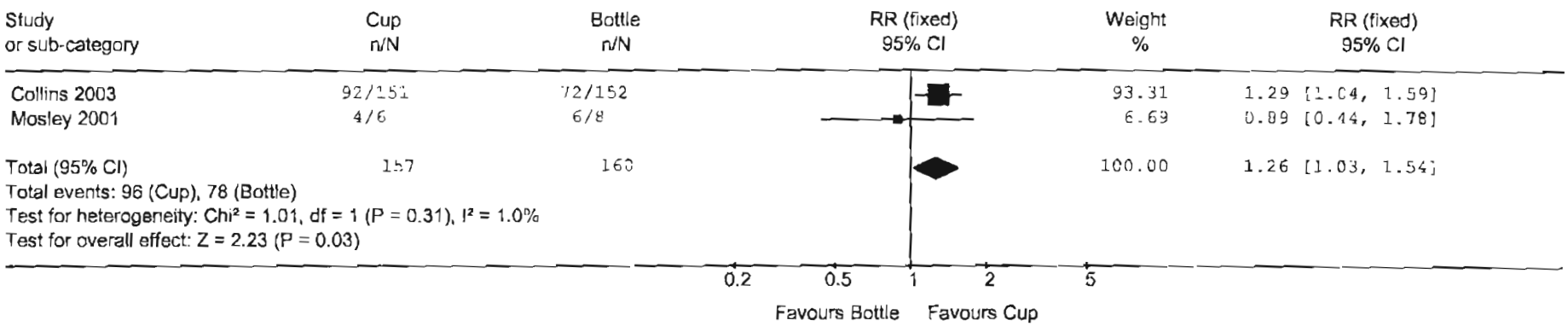


Figure 10.22 Fully breast feeding, Tube alone versus Bottle

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: Tube alone versus Bottle
Outcome: Fully breast feeding on discharge home

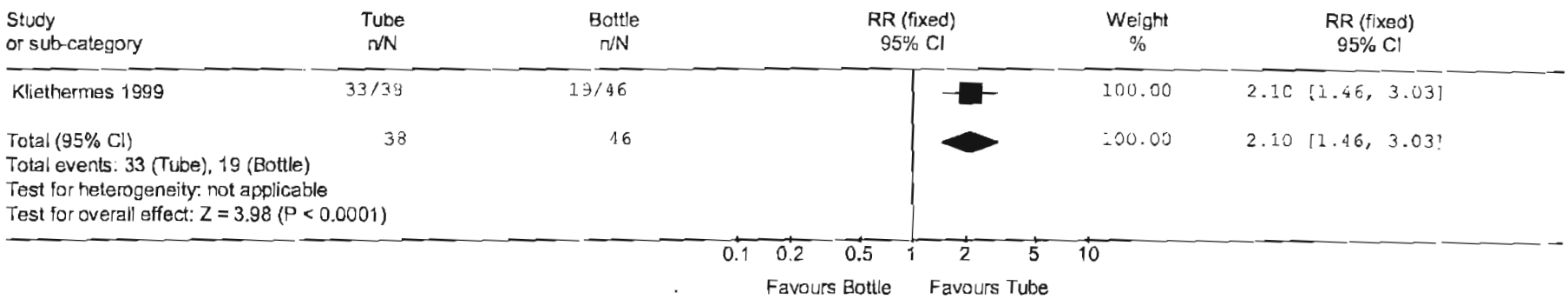


Figure 10.23 Weight gain, No Bottle versus Bottle

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (all trials)
Outcome: Weight gain (g/kg/day)

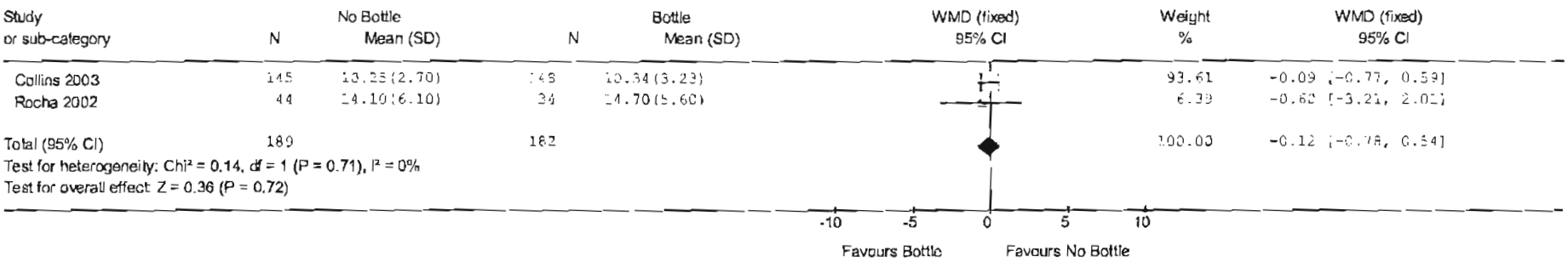


Figure 10.24 Weight gain, No Bottle versus Bottle, < 28 weeks gestation

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (<28 weeks)
Outcome: Weight gain (g/kg/day)

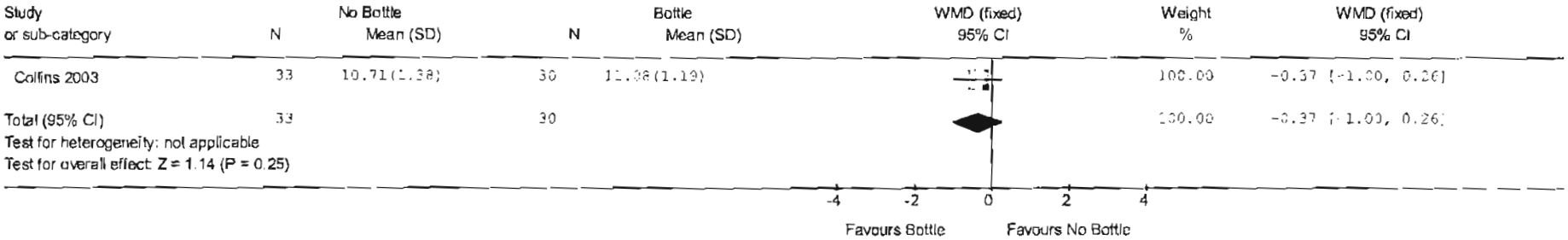


Figure 10.25 Weight gain, bottle versus no bottle, 28 - < 37 weeks gestation

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (28 to <37 weeks)
Outcome: Weight gain (g/kg/day)

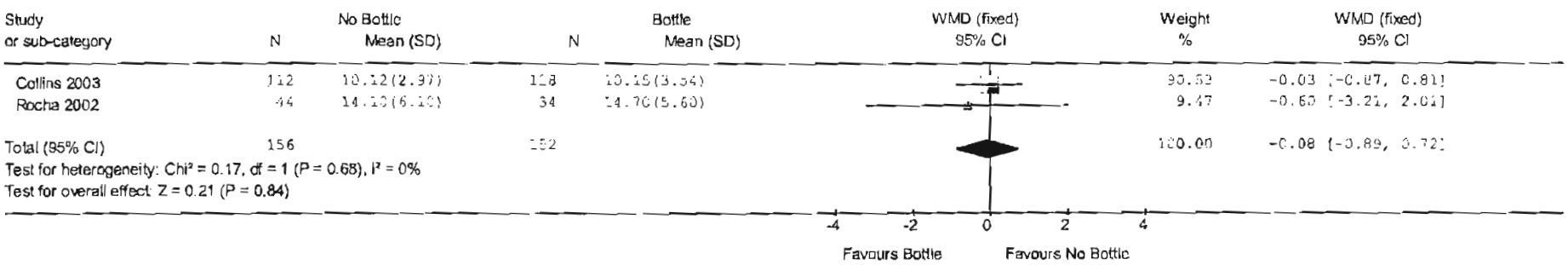


Figure 10.26 Length of hospitalisation, No Bottle versus Bottle

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (all trials)
Outcome: Length of hospitalisation

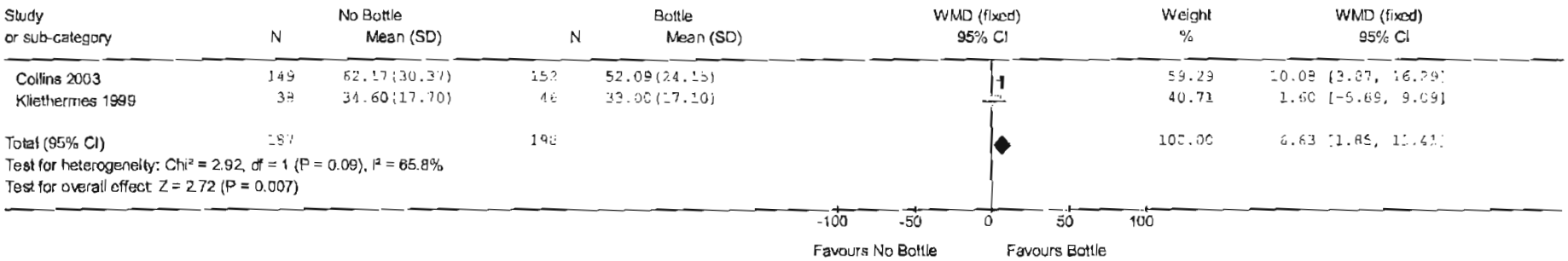


Figure 10.27 Length of hospitalisation, <28 weeks gestation

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (<28 weeks)
Outcome: Length of hospitalisation

Study or sub-category	No Bottle N	No Bottle Mean (SD)	Bottle N	Bottle Mean (SD)	WMD (fixed) 95% CI	Weight %	WMD (fixed) 95% CI
Collins 2003	35	98.29(17.63)	30	88.33(16.69)		100.00	9.96 [1.61, 18.31]
Total (95% CI)	35		30			100.00	9.96 [1.61, 18.31]

Test for heterogeneity: not applicable
Test for overall effect: Z = 2.34 (P = 0.02)

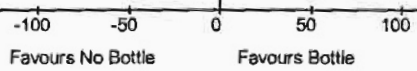


Figure 10.28 Length of hospitalisation, 28 to <37 weeks gestation

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (28 to <37 weeks)
Outcome: Length of hospitalisation

Study or sub-category	No Bottle N	No Bottle Mean (SD)	Bottle N	Bottle Mean (SD)	WMD (fixed) 95% CI	Weight %	WMD (fixed) 95% CI
Collins 2003	114	51.08(24.22)	122	43.18(15.97)		100.00	7.90 [2.63, 13.17]
Total (95% CI)	114		122			100.00	7.90 [2.63, 13.17]

Test for heterogeneity: not applicable
Test for overall effect: Z = 2.94 (P = 0.003)

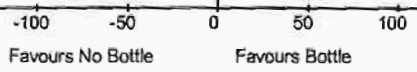


Figure 10.29 Length of hospitalisation, Cup versus Bottle

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: Cup versus Bottle
Outcome: Length of hospitalisation

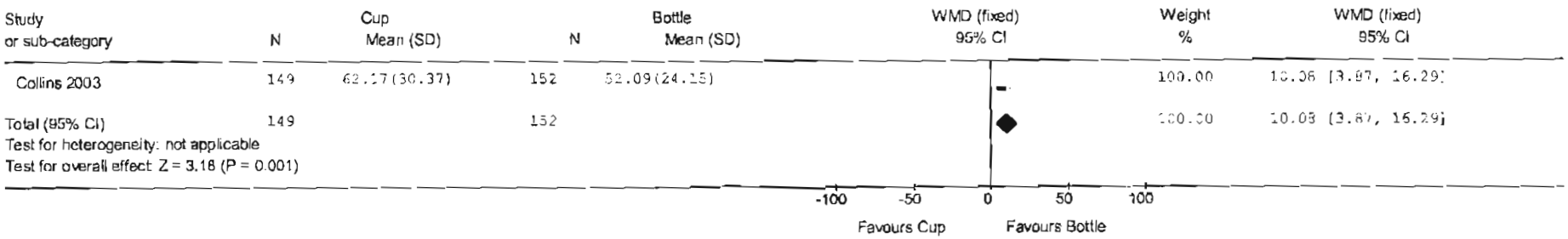


Figure 10.30 Length of hospitalisation, Tube alone versus Bottle

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: Tube alone versus Bottle
Outcome: Length of hospitalisation

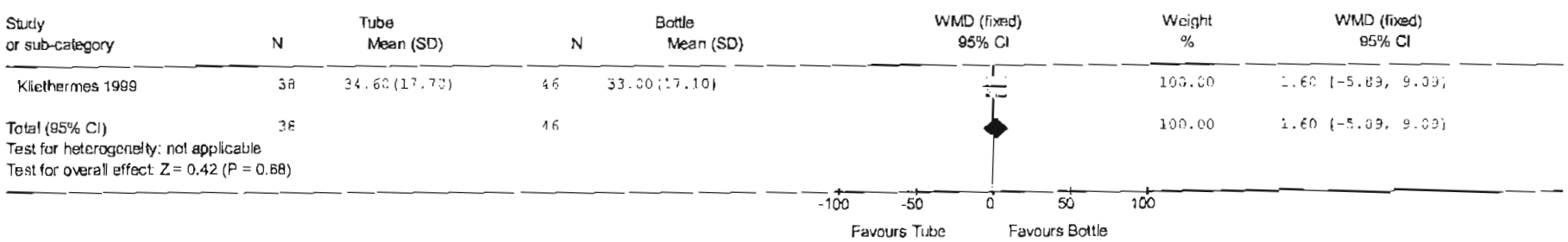


Figure 10.31 Duration of feed, No bottle versus Bottle

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (all trials)
Outcome: Duration of feed (minutes)

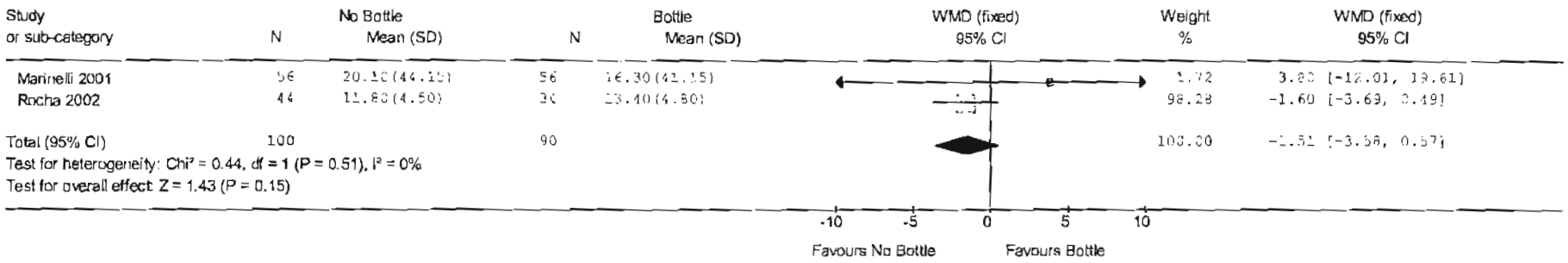


Figure 10.32 Duration of feed, No Bottle versus Bottle, 28 to < 37 weeks gestation.

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (28 to <37 weeks)
Outcome: Duration of feed (minutes)

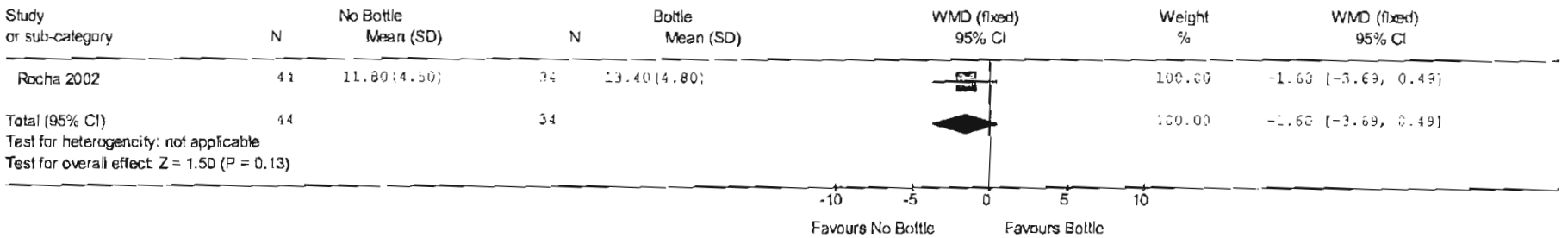


Figure 10.33 Heart rate, No Bottle versus Bottle

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (all trials)
Outcome: Heart rate

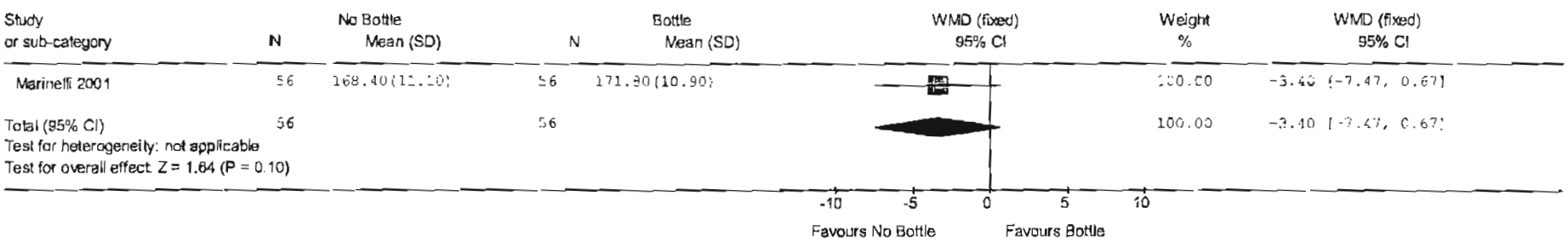
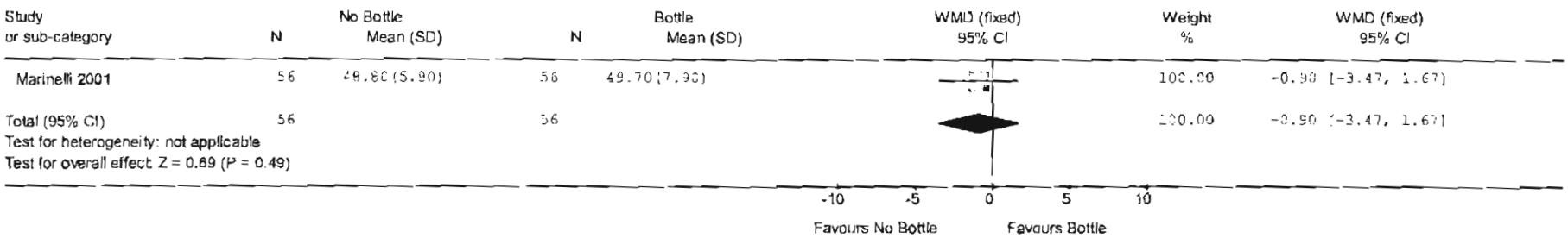


Figure 10.34 Respiratory rate, No Bottle versus Bottle

Review: Bottle feeding during the transition from tube to breast feeds in preterm infants.
Comparison: No Bottle versus Bottle (all trials)
Outcome: Respiratory Rate



Chapter 11. Conclusions

This thesis reports the investigation of the relationship between artificial teats (dummy and bottle) and breast feeding outcomes in preterm infants by a randomised controlled trial comparing bottles, cups and dummies in preterm infants less than 34 weeks gestation at birth, and by a systematic review of randomised controlled trials.

The results of the randomised controlled trial provide no evidence to support not using a dummy in preterm infants less than 34 weeks gestation as a strategy to increase breast feeding prevalence. Therefore, dummies can safely be used for preterm infants during hospitalisation, without fear of interfering with breast feeding outcomes. The results of the systematic review show that using a dummy does not reduce the time taken to reach all sucking feeds or the length of hospital stay. Parents need to be informed that there are no disadvantages to using a dummy during hospitalisation in the preterm infant population.

The results of the randomised controlled trial (with nearly half the participants non compliant) show that the use of cups significantly increases the proportion of infants discharged home fully breast feeding compared with partially and not breast feeding but there is no significant difference in the prevalence of 'any' breast feeding. The use of cups also significantly increases the risk of an increased time to reach all sucking feeds and length of hospital stay. Given the difficulty in staff and parent acceptance of cup feeding in this study, the lack of effect on the outcome 'any breast feeding', and the increase length of hospitalisation, it would be difficult to recommend the introduction of cup feeding into nurseries, except where staff are keen to use this modality. Ongoing audit would need to be conducted to measure the effect on length of hospital stay, and consideration given to early discharge programs with home support of gavage feeding.

The results from the systematic review show that not using a bottle in the preterm infant's transition to breast feeds has significant advantages for breast feeding outcomes and cardio respiratory stability. More research is needed on the method of 'no bottle'. There do not appear to be any negative effects of a tube alone approach in the transition to breast feeds, but a non significant increase in any breast feeding and a longer duration of time to full sucking feeds and length of stay with cup feeds.

There is a need for further trials in other centres to investigate the ideal method of a no bottle approach in the transition to breast feeds for preterm infants. Research is needed to assess if there is a critical point at which bottle feeds can be introduced without detriment to breast feeding outcomes. It is important that the most efficacious method of supplementing and complementing breast feeds in the transition from tube to breast feeding is established to enable women who choose to breast feed achieve their aim.

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Appendix I: Participating peripheral hospitals

Hospital	Town/Suburb
South Australia	
Barmera Hospital	Barmera
Blackwood Hospital	Belair
Ceduna Hospital	Ceduna
Flinders Medical Centre	Bedford Park
Gawler Health Service	Gawler
Kapunda Hospital	Kapunda
Lyell McEwin Health Service	Elizabeth Vale
Modbury Hospital	Modbury
Naracoorte Health Service	Naracoorte
Port Lincoln Health Services	Port Lincoln
Port Pirie Regional Health Service	Port Pirie
South Coast District Hospital	Victor Harbour
The Queen Elizabeth Hospital	Woodville
Wallaroo Hospital	Wallaroo
Western Hospital	Henley Beach
Northern Territory	
Alice Springs Hospital	Alice Springs
Royal Darwin Hospital	Darwin
Victoria	
Bairnsdale Hospital	Bairnsdale
Ballarat Base Hospital	Ballarat
Bendigo Hospital	Bendigo
Box Hill Hospital	Box Hill
Central Gippsland Base Hospital	Sale
Colac Community Health Services	Colac
Dandenong Hospital	Dandenong
Diamond Valley Community Hospital	Greensborough
Frankston Hospital	Frankston
Geelong Hospital	Geelong
Goulburn Valley Base Hospital	Shepparton
Hamilton Base Hospital	Hamilton

Kilmore & District Hospital	Kilmore
La Trobe Regional Hospital	Traralgon
Leongatha Hospital	Leongatha
Mitcham Private Hospital	Mitcham
Monash Medical Centre	Clayton
Mount Waverly Private Hospital	Mt Waverly
Mt Alexander Hospital	Castlemaine
Mt Alvernia Mercy Hospital	Bendigo
Northern Hospital	Epping
Northpark Private Hospital	Bundoora
Peninsula Private Hospital	Frankston
Sandringham & District Memorial Hospital	Sandringham
Seymour District Memorial Hospital	Seymour
South Eastern Private Hospital	Noble Park
St John of God Health Care	Geelong
Sunbury Private Hospital	Sunbury
Sunshine Hospital	St Albans
The Angliss Hospital	Upper Ferntree Gully
The Valley Private Hospital	Mulgrave
Wangaratta District Base Hospital	Wangaratta
Warnambool & District Base Hospital	Warnambool
Werribee Mercy Hospital	Werribee
West Gippsland Hospital	Warragul
Wimmera Base Hospital	Horsham
Wodonga Hospital	Wodonga

Appendix II: Cup feeding standard

STANDARD 2 - 18G

WOMEN'S AND CHILDREN'S HOSPITAL

NURSING AND MIDWIFERY CLINICAL STANDARDS

CUP FEEDING

RATIONALE:

1. Cup feeding provides an alternative method of feeding when supplementary or complementary feeds are necessary.
2. Cup feeding may be used:
   - for the premature baby's transition from tube to breastfeeds
   - when mother is unavailable for a breastfeed
   - to minimise the risk of sucking confusion (real or theoretical)
   - for babies who are difficult to attach or showing signs of breast refusal.
3. Cup feeding stimulates tongue movement as the ability to extend the tongue is essential for stripping milk ducts during breastfeeding.
4. **A cup feed does not replace a breast feed.**
   (It is optimal for the sucking feed to be a breast feed).

STANDARD STATEMENT:

The Nurse or Midwife (Mothercraft/Enrolled or Registered) will ensure that:

1. The cup feed is given slowly and safely to the neonate.
2. The parents understand the rationale for a cup feed.

EQUIPMENT:

- Sterile gavage cup.
- Breast milk or formula
- Tissues/cloth nappy

PROCESS CRITERIA:

Skill Level: RM/MCN/EN

1. Collect equipment.
2. **If EBM is used, ensure correct milk is given by checking same against baby's ID band with another staff member, or parent of the baby,** ***and signed by both people on the nutritional flowchart or observation/feeding chart.***

   Pour measured amount of EBM/formula into gavage cup. In SCBU/NICU, relabel the container.
3. Employ universal precautions.
4. Wrap baby securely in blanket or cloth nappy, to prevent hands knocking the cup.
5. Place cloth nappy or tissues under the baby's chin.
6. Explain the procedure to the parent.
7. Support the baby in an upright sitting position on your lap.
8. Rest the cup against neonate's bottom lip and chin.
9. Direct the rim of the cup towards the corners of the upper lip and gums, with it gently touching/resting on the lower lip.
10. Allow the neonate to swallow, and rest as necessary. It is important to let the baby take as much as s/he needs in her/his own time. (Initially a preterm baby may only take a small amount from the cup -maybe 5- 10 mls).

    This milk should not be poured into the baby's mouth.
11. It is not necessary to remove the cup when the baby stops drinking.
12. Dewind as necessary.
13. In NICU/SCBU, top the baby up if necessary via gavage.
14. Chart amount taken and method of feeding.
15. Settle baby in cot.
16. Dispose of used equipment appropriately.

OUTCOME STATEMENT:

1. The baby receives the correct EBM or formula via the cup.
2. The baby cup feeds at his or her own pace and receives the prescribed amount of milk.
3. The parent(s) understand the reasons for cup feeding.

Reference:

Lang S, Lawrence C, Orme R "Cup- Feeding : An Alternative Method of Infant Feeding" in Breastfeeding Review, vol 3, No. 1, April 1995

"Infant Feeding Guidelines for Health Workers" NH&MRC 1996

Appendix III: Consent form

THE BCD

(BOTTLES, CUPS & DUMMIES)

TRIAL

I, the undersigned (please print name in full)

.....

hereby consent to my baby's and my involvement in the research project entitled:

Transition to breast feeds for premature infants; does the use of artificial teats (dummy or bottle) affect breast feeding success?

I acknowledge that the nature, purpose and contemplated effects of the project so far as it affects me and my son/daughter, have been fully explained to my satisfaction by the research worker and my consent is given voluntarily.

I understand that the effect of artificial teats on the success of breast feeding in premature babies has not been established. The detail of bottle and cup feeding with relation to breast feeding my son/daughter has been explained to me. I understand that my baby and I will be randomly allocated (50% chance) to receive a dummy or not, then randomly allocated (50% chance) to receive cup or bottle supplements.

I have been given the opportunity to have a member of family or a friend present while the project was explained to me.

I am informed that no information regarding my son/daughter's or my medical history will be divulged and the results of this project involving myself and my son/daughter will not be published so as to reveal our identity.

I understand that the involvement of myself and my son/daughter in this project will not affect any relationship with my medical and midwifery/nursing advisers in their management of my baby's health. I also understand that I am free to withdraw from the project at any stage. I understand that this project has the approval of the Women's and Children's Hospital Ethics committee

Signed: .....

Address: .....

.....

Witness: .....

Research Worker .....

Date: ...../...../.....

Appendix IV: Maternal questionnaire

Questionnaire No. 1 Database record No. ☐☐☐☐

Study No. ☐☐☐☐

The BCD Trial

Thank you for participating in the BCD (bottles, cups & dummies) trial. This trial is being conducted to form a better understanding of the many issues around breast feeding premature babies. We would be very grateful if you could take a few minutes to answer the following questions. This information will be kept strictly confidential. ***The questionnaire can be returned via the enclosed envelope.***

Date: __/__/__

1. Early in your pregnancy had you decided to breast feed your baby?

(please tick one) YES ☐ *(go to Q2)*

NO ☐ *(go to Q3)*

2. For what length of time had you planned to breast feed your baby?

(please tick one)

6 weeks or less ☐

More than 6 weeks to 3 months ☐

More than 3 months to 6 months ☐

More than 6 months ☐

Don't know/unsure ☐

(Now go to Q3).

3. Now that you have had your baby how long would you like to breast feed?

(please tick one)

6 weeks or less ☐

More than 6 weeks to 3 months ☐

More than 3 months to 6 months ☐

More than 6 months ☐

Don't know/unsure ☐

4. What is the longest you have ever breast fed?

(please tick one)

Never ☐

6 weeks or less ☐

More than 6 weeks to 3 months ☐

More than 3 months to 6 months ☐

More than 6 months ☐

(please turn over)

The following questions will provide us with background information to ensure we have a representative sample of all women who choose to breast feed their premature baby.

5. What is your level of education?

(please tick one)
- Incomplete High School ☐
- Complete High School ☐
- Tertiary ☐

6. What is the major source of your household income?

(please tick one)
- Part time work ☐
- Benefits ☐
- Full time work ☐

7. Do you plan to undertake paid work some time during your baby's first 12 months?

- Yes ☐ *(go to Q8)*
- No ☐ *(go to Q12)*

8. Do you plan to work -

(please tick one)
- Full time ☐
- Part time ☐

(Now go to Q9)

9. What age will your baby be when you plan to undertake paid work?

(please tick one)
- Less than 3 months old ☐
- Between 3 months & 6 months old ☐
- Between 6 months and 12 months old ☐

10: Will your baby still be in hospital when you undertake paid work?

- Yes ☐ *(go to Q11)*
- No ☐ *(go to Q12)*

11: If your baby is still in hospital when you undertake paid work, will you stop work once your baby is discharged home?

- Yes ☐ *(go to Q12)*
- No ☐ *(go to Q12)*

12. Do you live with another adult (eg., partner/ husband/parent/friend)?

- Yes ☐
- No ☐

Thank you for your valuable contribution to this important trial

If you have any questions please contact:
Carmel Collins,
Dept. Nursing & Midwifery Research
& Practice Development

Women's & Children's Hospital
72 King William Rd
North Adelaide 5006

Tel: 82047000

Appendix V: Discharge data sheet (discharge home/transfer from recruiting hospital)

Database record No ☐☐☐☐

Study No. ☐☐☐☐

☐ group A *(cup, no dummy)* ☐ group C *(bottle, no dummy)*

☐ group B *(cup, dummy)* ☐ group D *(bottle, dummy)*

Patient sticker

THE BCD TRIAL

DISCHARGE/TRANSFER from WCH

Maternal: age ☐☐

Parity G☐ P☐

Birth Weight ☐.☐☐☐ kg

Total days WCH ☐☐☐

SEPARATION ☐

1. Discharge home
2. Transfer - Date __/__/__
   - Dest. _____
3. NND <28 days
4. PNND >28 days

Discharge: date __/__/__

weight ☐.☐☐☐ kg

length ☐☐.☐ cm

HC ☐☐.☐ cm

Mode delivery ☐

Plurality ☐

Birth Order ☐

Ethnicity ☐

RESPIRATORY

FiO_2 duration days ☐☐☐

PIP duration days ☐☐☐

CPAP durat. days ☐☐☐

Discharged home on O_2 Y / N

Main Resp diagnosis _____

CNS

PVT/VH

Grade L) _____

Grade R) _____

PVLE _____

GASTRO-INTESTINAL

NEC Y / N

Other _____

BREAST MILK

(on discharge/transfer) Y / N

IF NO:

Date stopped __/__/__

No. days exp/BF ☐☐☐

Commenced oral feeds:
breast/bottle/cup feeds Y / N

IF YES:

Exclusive _____

> 80% _____

80% - 50% _____

49% - 20% _____

< 20% _____

Token _____

FEEDING REGIME on TRANSFER

No. feeds/24 hrs ☐ No. bottle ☐

No. gavage ☐ No. cup ☐

No. breast ☐

Date of final gavage feed: __/__/__

No. days to final gavage: ☐☐☐

NO DUMMY groups (A&C)

Was a dummy introduced Y / N

IF YES:

Date introduced: __/__/__

Reason:

Will not settle ☐

Insufficient staff time ☐

Parents requested ☐

Unknown ☐

Other _____

CUP GROUPS (groups A&B)

Did the baby change to bottle supps/comps Y / N

IF YES:

Error/Overlooked ☐

Baby not satisfied/wouldn't settle ☐

Parents requested ☐

Staff initiated ☐

Any other issues related to cup feeding:

Earlier discharge: ☐

Mum boarded in residential accom. ☐

Comments/Other

_____

_____

_____

_____

BREAST FEEDING frequency on DISCHARGE/24 hrs

5 - 7 ☐

8 - 10 ☐

> 10 ☐

COMPS (EBM/form. After BF)

Method & frequency/24 hrs.

Nil ☐

Cup ☐

Bottle ☐

Gavage ☐

SUPPS (BF replaced with EBM/Form)

Method & frequency/24 hrs:

Nil ☐

Cup ☐

Bottle ☐

Gavage ☐

ADVERSE EVENTS:

Aspiration Y / N

Other _____

SUPPLY LINE Y / N

Post discharge death Y / N

Cause: _____

Neonatal data sheet (discharge home from peripheral hospital)

HOSPITAL:

UNo:

THE BCD TRIAL

DISCHARGE HOME FROM PERIPHERAL HOSPITAL

No. days periph hosp ☐☐☐

TOTAL hosp days ☐☐☐

SEPARATION ☐

1. Discharge home
2. Transfer - Date __/__/__
   - Dest. _____
3. NND <28 days
4. PNND >28 days

Discharge: date __/__/__

weight ☐.☐☐☐ kg

length ☐☐.☐ cm

HC ☐☐.☐ cm

RESPIRATORY

FiO_2 duration days ☐☐☐

Date of final FiO_2 __/__/__

Discharged home on O_2 Y / N

BREAST MILK

(on discharge) Y / N

IF NO:

Date stopped __/__/__

No. days exp/BF ☐☐☐

IF YES:

Exclusive _____

> 80% _____

80% - 50% _____

49% - 20% _____

<20% _____

Token _____

Date of final gavage feed: __/__/__

No. days to final gavage: ☐☐☐

NO DUMMY groups (A&C)

Was a dummy introduced Y / N

IF YES:

Date introduced: __/__/__

Reason:

Will not settle ☐

Insufficient staff time ☐

Parents requested ☐

Unknown ☐

Other _____

CUP GROUPS (groups A&B)

Did the baby change to bottle supps/comps Y / N

IF YES:

Error/Overlooked ☐

Baby not satisfied/wouldn't settle ☐

Parents requested ☐

Staff initiated ☐

Any other issues related to cup feeding:

Earlier discharge: ☐

Mum boarded in residential accom. ☐

Comments/Other

.....

.....

.....

.....

BREAST FEEDING frequency on Discharge 24 hrs

5 - 7 ☐

8 - 10 ☐

> 10 ☐

COMPS (EBM/form, after BF)

Method & frequency/24 hrs:

Nil ☐

Cup ☐

Bottle ☐

Gavage ☐

SUPPS (BF replaced with EBM/Form)

Method & frequency/24 hrs:

Nil ☐

Cup ☐

Bottle ☐

Gavage ☐

SUPPLY LINE Y / N

ADVERSE EVENTS:

Aspiration Y / N

Other _____

Post discharge death

Cause: _____

Appendix VI: Three month questionnaire (form 2A, 2B, 2C, 2D)

Form No. 2A

Study No: ☐☐☐☐
Database No: ☐☐☐☐

The BCD Trial

Thank you for participating in the BCD (bottles, cups & dummies) trial. Our aim is to form a more complete picture of the issues important in breastfeeding premature babies. We would be very grateful if you could answer the following questions as your responses will provide vital information that will help improve the care for women who choose to breastfeed their premature baby. Your responses remain important to us even if you are no longer breast feeding or expressing or if you aren't in the original group you were allocated to. Please return the form via the enclosed prepaid envelope. Thank you for your valuable contribution.

Date: __/__/__

1. Please indicate the type of milk, or combination of milks, that your baby has received in the past 24 hours
(please tick one)

breast milk only ☐ *...(go to Q 2)*
breast milk and formula ☐ *...(go to Q 3)*
formula only ☐ *(go to Q 5)*

2. Babies receiving breast milk only (ie no formula)
How many feeds did your baby receive in the last 24 hours? ☐

Of these breast milk feeds how many were:

a) direct Breast feeds? ☐
b) expressed breast milk (EBM) given by bottle? ☐
c) EBM given by cup? ☐
(Now go to Q 9)

3. Babies receiving breast milk and formula
Please tick which statement most closely describes the proportion of breast milk your baby receives:

a) More than half milk feeds are breast milk the rest are formula ☐
b) About half milk feeds are breast milk and half formula ☐
c) Less than half milk feeds are breast milk, the rest are formula ☐
(Now go to Q 4)

4. Babies receiving breast milk and formula.
How many milk feeds did your baby receive in the last 24 hours? ☐

Of these feeds how many were:

a) direct breast feeds? ☐
b) expressed breast milk (EBM) given by bottle ☐
c) EBM given by cup? ☐
d) formula given by bottle? ☐
e) formula given by cup? ☐
(go to Q 9)

5. If you are not breast feeding your baby, how old was your baby when you stopped breast feeding or expressing?

Less than 1 month ☐
1 month to less than 2 months ☐
2 months to less than 3 months ☐
3 months to less than 4 months ☐
4 months to less than 5 months ☐
5 months to less than 6 months ☐
6 months to less than 7months ☐
(go to Q 6)

6. Did you stop expressing before your baby started breast feeding?

Yes ☐ *(go to Q 7)*
No ☐ *(go to Q 8)*

7. What was your reason or reasons for stopping expressing?
(Please tick as many reasons that apply)

My milk supply did not increase enough to meet my baby's needs. ☐
I only wanted to express while my baby was sick. ☐
I didn't like expressing ☐
I found expressing difficult. ☐
I found it difficult to fit in expressing with other demands on my time (children, travelling to hospital etc) ☐
I felt embarrassed expressing ☐
I did not really want to breast feed ☐
Other (please specify) ☐

.....
.....
.....
.....
.....
.....

(Now go to Q 9)

8. What were your reason or reasons for stopping breastfeeding?
(Please tick as many reasons that apply)

I went back to work ☐
My baby was sleepy at the breast ☐
It was difficult to express at my workplace (not enough time/facilities) ☐
My baby was fussy during breast feeding ☐
My baby was fussy after breast feeding ☐
I wanted to be able to sleep longer ☐
My baby had a weak suck ☐
I had a medical reason ☐
(please specify).....
My baby refused the breast ☐
My baby had a poor weight gain ☐
I had sore nipples ☐
My baby took the bottle better ☐
I didn't feel my milk was good enough ☐
My baby breast fed too frequently ☐
I thought my baby wasn't getting enough ☐
I wanted to make sure my baby got enough ☐
My doctor advised me to stop ☐
I didn't feel I had enough milk ☐
I didn't really like breast feeding ☐
I didn't really want to breast feed ☐
Other *(please specify)* ☐

.....
.....
.....
.....

(go to Q 9)

9 Did you have skin-to-skin contact with your baby in hospital? (Holding your baby naked, except for a nappy, against your chest)

Yes ☐ No ☐ Don't know/Unsure ☐

↳ **If YES:** Approximately how frequently?

Daily ☐
About every second day ☐
About once per week ☐
Other *(please specify)* ☐

.....
.....
.....

Do you have any comments on skin-to-skin contact?.....
.....
.....
.....
.....

10. Did you take a drug called Maxalon for your milk supply?

NO ☐ *(go to Q 11)*
YES ☐ → If YES how many courses did you take?
Did you find it elpful?.....
.....
.....
.....

(go to Q 11)

11. Did you use a nipple shield when breast feeding your baby?

Not applicable ☐ *(go to Q 12)*
Yes ☐ No ☐ *(go to Q 12)*

↳ **If YES:** Did you stop using the nipple shield BEFORE your baby was discharged from hospital?

Yes ☐ *(go to Q 12)*
No ☐old was your baby when you stopped using a nipple shield?

Less than 1 month ☐
1 month to less than 2 months ☐
2 months to 3 months ☐
Still using a nipple shield ☐

(continued next page)

12. **Did you use a SUPPLY LINE (or supplemental feeding device) when breast feeding your baby?**

Yes ☐ No ☐ *(go to Q 13)*

↳ **If YES:** Did you find this helpful? Yes ☐ No

Please comment:.....

.....

.....

.....

(go to Q 13)

13. **a) Have you ever been a smoker?**

Yes ☐ No ☐

b) Are you a smoker now?

Yes ☐ No ☐

14. **How much does your baby weigh now?**

__ __ kg

Date weighed: ..../...../.....

15. **Please indicate your level of agreement with the following statement by circling ONE of the responses:**

"My partner/husband has been very supportive of me breastfeeding our baby?"

Strongly disagree / Disagree / Agree / Strongly Agree / Don't know / Not applicable

Comment:.....

.....

.....

.....

16. **You and your baby were allocated to the CUP and NO DUMMY group**

a) Were you happy with the group you were allocated to?

Yes ☐ No ☐

Neither happy nor unhappy ☐

Comment:.....

.....

.....

.....

.....

.....

.....

b) Did your baby change to receiving BOTTLES while in hospital?

Yes ☐ No ☐ *(go to Q 16c)*

↳ **If YES:** What was the reason or reasons for changing

(tick whichever box or boxes apply)

I was advised by the nurse/midwife ☐

I was advised by the doctor ☐

It was my decision ☐

I was influenced by my husband/partner ☐

I was influenced by my family ☐

My baby was not satisfied with cup feeds ☐

I didn't really like cup feeds ☐

Other (please specify) ☐

.....

.....

.....

.....

.....

.....

.....

.....

c) Did your baby change to having a dummy while in hospital?

Yes ☐ No ☐ *(go to Q 17)*

↳ **If YES:** What was the reason or reasons for giving your baby a dummy?

(tick whichever box or boxes apply)

I was advised by the nurse/midwife ☐

I was advised by the doctor ☐

I was influenced by my husband/partner ☐

I was influenced by my family ☐

My baby was unsettled without a dummy ☐

I decided I wanted my baby to have a dummy ☐

I thought it might teach my baby to suck ☐

Other (please specify)..... ☐

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17. **Does your baby use a dummy now?**

Yes ☐ No ☐

With the following 4 questions you may like to offer your thoughts or opinions on:

- *the BCD trial OR*
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(If you require further room, please attach separate pages.)

18. What advice would you give to other parents of preterm babies?

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I have felt happy:

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This would mean: "I have felt happy most of the time during the past week"

If the results of this part of the questionnaire suggest that you may be depressed would you like to be contacted Yes ☐ **No** ☐

In the past 7 days:

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- not quite so much now ☐
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2. I have looked forward with enjoyment to things:-

- as much as I ever did ☐
- rather less than I used to ☐
- definitely less than I used to ☐
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3. I have blamed myself unnecessarily when things went wrong:-

- yes, most of the time ☐
- yes, some of the time ☐
- not very often ☐
- no, never ☐

4. I have been anxious or worried for no good reason:-

- no, not at all ☐
- hardly ever ☐
- yes, sometimes ☐
- yes, very often ☐

5. I have felt scared or panicky for no very good reason:-

- yes, quite a lot ☐
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- no, most of the time I have coped quite well ☐
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- yes, quite often ☐
- not very often ☐
- no, not at all ☐

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- only occasionally ☐
- no, never ☐

10. The thought of harming myself has occurred to me:-

- yes, quite often ☐
- sometimes ☐
- hardly ever ☐
- never ☐

(EDINBURGH POSTNATAL DEPRESSION SCALE (EPDS)
JL Cox. JM Holden, R Sagovsky)

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Women's & Children's Hospital
72 King William Rd
North Adelaide. 5006.

Form No. 2B

Study No: ☐☐☐☐
Database No: ☐☐☐☐

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Date: / /

1. Please indicate the type of milk, or combination of milks, that your baby has received in the past 24 hours
(please tick one)

breast milk only ☐ *...(go to Q 2)*
breast milk and formula ☐ *...(go to Q 3)*
formula only ☐ *(go to Q 5)*

2. Babies receiving breast milk only (ie no formula)
How many feeds did your baby receive in the last 24 hours? ☐

Of these breast milk feeds how many were:
a) direct Breast feeds? ☐
b) expressed breast milk (EBM) given by bottle? ☐
c) EBM given by cup? ☐
(Now go to Q 9)

3. Babies receiving breast milk and formula
Please tick which statement most closely describes the proportion of breast milk your baby receives:

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b) About half milk feeds are breast milk and half formula ☐
c) Less than half milk feeds are breast milk, the rest are formula ☐
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How many milk feeds did your baby receive in the last 24 hours? ☐

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a) direct breast feeds? ☐
b) expressed breast milk (EBM) given by bottle ☐
c) EBM given by cup? ☐
d) formula given by bottle? ☐
e) formula given by cup? ☐
(go to Q 9)

5. If you are not breast feeding your baby, how old was your baby when you stopped breast feeding or expressing?

Less than 1 month ☐
1 month to less than 2 months ☐
2 months to less than 3 months ☐
3 months to less than 4 months ☐
4 months to less than 5 months ☐
5 months to less than 6 months ☐
6 months to less than 7months ☐
(go to Q 6)

6. Did you stop expressing before your baby started breast feeding?

Yes ☐ *(go to Q 7)*
No ☐ *(go to Q 8)*

7. What was your reason or reasons for stopping expressing?
(Please tick as many reasons that apply)
My milk supply did not increase enough to meet my baby's needs. ☐
I only wanted to express while my baby was sick. ☐
I didn't like expressing ☐
I found expressing difficult ☐
I found it difficult to fit in expressing with other demands on my time (children, travelling to hospital etc) ☐
I felt embarrassed expressing ☐
I did not really want to breast feed ☐
I didn't really like breast feeding ☐
Other ☐
(please specify).....
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(Now *go to Q 9)*

8. What were your reason or reasons for stopping breastfeeding?
(Please tick as many reasons that apply)
I went back to work ☐
My baby was sleepy at the breast ☐
It was difficult to express at my workplace (not enough time/facilities) ☐
My baby was fussy during breast feeding ☐
My baby was fussy after breast feeding ☐
I wanted to be able to sleep longer ☐
My baby had a weak suck ☐
I had a medical reason ☐
(please specify).....
My baby refused the breast ☐
My baby had a poor weight gain ☐
I had sore nipples ☐
My baby took the bottle better ☐
I didn't feel my milk was good enough ☐
My baby breast fed too frequently ☐
I thought my baby wasn't getting enough ☐
I wanted to make sure my baby got enough ☐
My doctor advised me to stop ☐
I didn't feel I had enough milk ☐
I didn't really like breast feeding ☐
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Other *(please specify)* ☐
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(go to Q 9)

9. Did you have skin-to-skin contact with your baby in hospital? (Holding your baby naked, except for a nappy, against your chest)
Yes ☐ No ☐ Don't know/Unsure ☐
↳ **If YES:** Approximately how frequently?
Daily ☐
About every second day ☐
About once per week ☐
Other *(please specify)* ☐
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Do you have any comments on skin-to-skin contact?.....
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10. Did you take a drug called Maxalon for your milk supply?
NO ☐ *(go to Q 11)*
YES ☐ ➔ If YES how many courses did you take?
Did you find it elpful?.....
.....
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(go to Q 11)

11. Did you use a nipple shield when breast feeding your baby?
Not applicable ☐ *(go to Q 12)*
Yes ☐ No ☐ *(go to Q 12)*
↳ **If YES:** Did you stop using the nipple shield BEFORE your baby was discharged home from hospital?
Yes ☐ *(go to Q 12)*
No ☐
↳ **If NO:** How old was your baby when you stopped using a nipple shield?
Less than 1 month ☐
1 month to less than 2 months ☐
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12. Did you use a SUPPLY LINE (or supplemental feeding device) when breast feeding your baby?

Yes ☐ No ☐ *(go to Q 13)*

↳ **If YES:** Did you find this helpful?

Yes ☐ No ☐

Please comment:.....

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(go to Q 13)

13. a) Have you ever been a smoker?

Yes ☐ No ☐

b) Are you a smoker now?

Yes ☐ No ☐

14. How much does your baby weigh now?

___ __ kg

Date weighed: ...../...../.....

15. Please indicate your level of agreement with the following statement by circling ONE of the responses:

"My partner/husband has been very supportive of me breastfeeding our baby?"

Strongly disagree / Disagree / Agree / Strongly Agree / Don't know / Not applicable

Comment:.....

.....

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.....

16. You and your baby were allocated to the CUP and DUMMY group

a) Were you happy with the group you were allocated to?

Yes ☐ No ☐

Neither happy nor unhappy ☐

Comment:.....

.....

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.....

.....

b) Did your baby change to receiving BOTTLES while in hospital?

Yes ☐ No ☐ *(go to Q 17)*

↳ **If YES:** What was the reason or reasons for changing

(tick whichever box or boxes apply)

I was advised by the nurse/midwife ☐

I was advised by the doctor ☐

It was my decision ☐

I was influenced by my husband/partner ☐

I was influenced by my family ☐

My baby was not satisfied with cup feeds ☐

I didn't really like cup feeds ☐

Other (please specify) ☐

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Form No. 2C

Study No: ☐☐☐☐

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(go to Q 9)

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5 months to less than 6 months ☐
6 months to less than 7months ☐
(go to Q 6)

6. Did you stop expressing before your baby started breast feeding?

Yes ☐ *(go to Q 7)*
No ☐ *(go to Q 8)*

7. What was your reason or reasons for stopping expressing?
(Please tick as many reasons that apply)

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I found expressing difficult. ☐
I found it difficult to fit in expressing with other demands on my time (children, travelling to hospital etc) ☐
I felt embarrassed expressing ☐
I did not really want to breast feed ☐
Other ☐
(please pecify).....
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I wanted to be able to sleep longer ☐
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I had a medical reason ☐
(please specify).....
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My baby took the bottle better ☐
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I thought my baby wasn't getting enough ☐
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My doctor advised me to stop ☐
I didn't feel I had enough milk ☐
I didn't really like breast feeding ☐
(continued)

I didn't really want to breast feed ☐
Other *(please specify)* ☐
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(go to Q 9)

9. Did you have skin-to-skin contact with your baby in hospital? (Holding your baby naked, except for a nappy, against your chest)

Yes ☐ No ☐ Don't know/Unsure ☐

↳ **If YES:** Approximately how frequently?

Daily ☐
About every second day ☐
About once per week ☐
Other *(please specify)* ☐
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Do you have any comments on skin-to-skin contact?.....
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10. Did you take a drug called Maxalon for your milk supply?

NO ☐ *(go to Q 11)*
YES ☐ → If YES how many courses did you take? _____
Did you find it helpful?.....
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11. Did you use a nipple shield when breast feeding your baby?

Not applicable ☐ *(go to Q 12)*
Yes ☐ No ☐ *(go to Q 12)*

↳ **If YES:** Did you stop using the nipple shield BEFORE your baby was discharged home from hospital?

(continued next page)

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Yes ☐ No ☐

Please comment:.....
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(go to Q 13)

13. a) Have you ever been a smoker?

Yes ☐ No ☐

b) Are you a smoker now?

Yes ☐ No ☐

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____ kg

Date weighed: ...../...../.....

15. Please indicate your level of agreement with the following statement by circling ONE of the responses:

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Strongly disagree / Disagree / Agree / Strongly Agree / Don't know / Not applicable

Comment:.....
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16. You and your baby were allocated to the BOTTLE and NO DUMMY group

a) Were you happy with the group you were allocated to?

Yes ☐ No ☐

Neither happy nor unhappy ☐

Comment:.....
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Yes ☐ No ☐ *(go to Q 17)*

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I was influenced by my family ☐
My baby was unsettled without a dummy ☐
I decided I wanted my baby to have a dummy ☐
I thought it might teach my baby to suck ☐
Other (please specify)..... ☐

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Form No. 2D

Study No: ☐☐☐☐
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b) expressed breast milk (EBM) given by bottle? ☐
c) EBM given by cup? ☐
(Now go to Q 9)

3. Babies receiving breast milk and formula
Please tick which statement most closely describes the proportion of breast milk your baby receives:

a) More than half milk feeds are breast milk the rest are formula ☐
b) About half milk feeds are breast milk and half formula ☐
c) Less than half milk feeds are breast milk, the rest are formula ☐
(Now go to Q 4)

4. Babies receiving breast milk and formula
How many milk feeds did your baby receive in the last 24 hours? ☐

Of these feeds how many were:
a) direct breast feeds? ☐
b) expressed breast milk (EBM) given by bottle ☐
c) EBM given by cup? ☐
d) formula given by bottle? ☐
e) formula given by cup? ☐
(go to Q 9)

5. If you are not breast feeding your baby, how old was your baby when you stopped breast feeding or expressing?
Less than 1 month ☐
1 month to less than 2 months ☐
2 months to less than 3 months ☐
3 months to less than 4 months ☐
4 months to less than 5 months ☐
5 months to less than 6 months ☐
6 months to less than 7months ☐
(go to Q 6)

6. Did you stop expressing before your baby started breast feeding?
Yes ☐ *(go to Q 7)*
No ☐ *(go to Q 8)*

7. What was your reason or reasons for stopping expressing?
(Please tick as many reasons that apply)

My milk supply did not increase enough to meet my baby's needs. ☐
I only wanted to express while my baby was sick. ☐
I didn't like expressing ☐
I found expressing difficult. ☐
I found it difficult to fit in expressing with other demands on my time (children, travelling to hospital etc) ☐
I felt embarrassed expressing ☐
I did not really want to breast feed ☐
Other ☐
(please pecify).....
.....
.....
.....
.....
.....
(Now *go to Q 9)*

8. What were your reason or reasons for stopping breastfeeding?
(Please tick as many reasons that apply)

I went back to work ☐
My baby was sleepy at the breast ☐
It was difficult to express at my workplace (not enough time/facilities) ☐
My baby was fussy during breast feeding ☐
My baby was fussy after breast feeding ☐
I wanted to be able to sleep longer ☐
My baby had a weak suck ☐
I had a medical reason ☐
(please specify).....
My baby refused the breast ☐
My baby had a poor weight gain ☐
I had sore nipples ☐
My baby took the bottle better ☐
I didn't feel my milk was good enough ☐
My baby breast fed too frequently ☐
I thought my baby wasn't getting enough ☐
I wanted to make sure my baby got enough ☐
My doctor advised me to stop ☐
I didn't feel I had enough milk ☐
I didn't really like breast feeding ☐
(continued)

I didn't really want to breast feed ☐
Other *(please specify)* ☐
.....
.....
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.....
.....
.....
(go to Q 9)

9. Did you have skin-to-skin contact with your baby in hospital? (Holding your baby naked, except for a nappy, against your chest)

Yes ☐ No ☐ Don't know/Unsure ☐

↳ **If YES:** Approximately how frequently?

Daily ☐
About every second day ☐
About once per week ☐
Other *(please specify)* ☐
.....
.....
.....

Do you have any comments on skin-to-skin contact?.....
.....
.....
.....
.....

10. Did you take a drug called Maxalon for your milk supply?

NO ☐ *(go to Q 11)*
YES ☐ → If YES how many courses did you take? ____
Did you find it helpful?.....
.....
.....
.....
.(go to Q 11)

11. Did you use a nipple shield when breast feeding your baby?

Not applicable ☐ *(go to Q 12)*
Yes ☐ No ☐ *(go to Q 12)*

↳ **If YES:** Did you stop using the nipple shield BEFORE your baby was discharged home from hospital?

(continued next page)

Yes ☐ *(go to Q 12)*
No ☐

If NO: How old was your baby when you stopped using a nipple shield?

Less than 1 month ☐
1 month to less than 2 months ☐
2 months to 3 months ☐
Still using a nipple shield ☐

12. Did you use a SUPPLY LINE (or supplemental feeding device) when breast feeding your baby?

Yes ☐ No ☐ *(go to Q 13)*

If YES: Did you find this helpful?

Yes ☐ No ☐

Please comment:.....
.....
.....
.....

(go to Q 13)

13. a) Have you ever been a smoker?

Yes ☐ No ☐

b) Are you a smoker now?

Yes ☐ No ☐

14. How much does your baby weigh now?

____ kg

Date weighed: ...../...../.....

15. Please indicate your level of agreement with the following statement by circling ONE of the responses:

"My partner/husband has been very supportive of me breastfeeding our baby?"
Strongly disagree / Disagree / Agree / Strongly Agree / Don't know / Not applicable
Comment:.....
.....
.....
.....

16. You and your baby were allocated to the BOTTLE and DUMMY group
Were you happy with the group you were allocated to?

Yes ☐ No ☐
Neither happy nor unhappy ☐
Comment:.....
.....
.....
.....
.....
.....
.....
.....

17. Does your baby use a dummy now?

Yes ☐ No ☐

With the following 4 questions you may like to offer your thoughts or opinions on:

- *the BCD trial OR*
- *any aspect of your experience in having a premature baby.*

(If you require further room, please attach separate pages.)

18. What advice would you give to other parents of preterm babies?

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19. What advice would you give to the health care team (nurses, midwives, doctors)?

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(continued next page)

20. What advice would you give to family and friends?

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21. Are there any changes you would recommend for the hospital?

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.....

As you have been through a lot in having a premature baby we would also like to know how you are feeling now. Please tick the box of the answer which comes closest to how you have felt IN THE PAST 7 DAYS, not just how you feel today.

Here is an example already completed.
I have felt happy:

Yes, all the time ☐ *No, not very often* ☐
Yes, most of the time ☑ *No, not at all* ☐
This would mean: "I have felt happy most of the time during the past week"

If the results of this part of the questionnaire suggest that you may be depressed would you like to be contacted Yes ☐ No ☐

In the past 7 days:

1. I have been able to laugh and see the funny side of things:-

- as much as I always could ☐
- not quite so much now ☐
- definitely not so much now ☐
- not at all ☐

2. I have looked forward with enjoyment to things:-

- as much as I ever did ☐
- rather less than I used to ☐
- definitely less than I used to ☐
- hardly at all ☐

3. I have blamed myself unnecessarily when things went wrong:-

- yes, most of the time ☐
- yes, some of the time ☐
- not very often ☐
- no, never ☐

4. I have been anxious or worried for no good reason:-

- no, not at all ☐
- hardly ever ☐
- yes, sometimes ☐
- yes, very often ☐

5. I have felt scared or panicky for no very good reason:-

- yes, quite a lot ☐
- yes, sometimes ☐
- no, not much ☐
- no, not at all ☐

6. Things have been getting on top of me:-

- yes, most of the time I haven't been able to cope ☐
- yes, sometimes I haven't been coping as well as usual ☐
- no, most of the time I have coped quite well ☐
- no, I have been coping as well as ever ☐

7. I have been so unhappy that I have had difficulty sleeping:-

- yes, most of the time ☐
- yes, quite often ☐
- not very often ☐
- no, not at all ☐

8. I have felt sad or miserable:-

- yes, most of the time ☐
- yes, quite often ☐
- not very often ☐
- no, not at all ☐

9. I have been so unhappy that I have been crying:-

- yes, most of the time ☐
- yes, quite often ☐
- only occasionally ☐
- no, never ☐

10. The thought of harming myself has occurred to me:-

- yes, quite often ☐
- sometimes ☐
- hardly ever ☐
- never ☐

(EDINBURGH POSTNATAL DEPRESSION SCALE (EPDS)
JL Cox, JM Holden, R Sagovsky)

THANK YOU FOR YOUR TIME AND CONTRIBUTION TO THIS IMPORTANT RESEARCH - YOUR INVOLVEMENT WILL CERTIANLY MAKE A DIFFERENCE TO THE FUTURE CARE OF BREAST FEEDING PREMATURE BABIES.

We will notify you of the results of this research when they are available.

If you require further information or have any queries please do not to hesitate to contact:

Carmel Collins
Research Nurse/Midwife *Tel: 82047000*
Dept. Nursing & Midwifery Research
& Practice Developement
Women's & Children's Hospital
72 King William Rd
North Adelaide. 5006.

Appendix VII: Six month questionnaire (form 3A, 3B)

Form No. 3A

Study No: ☐☐☐☐

Database No: ☐☐☐☐

The BCD Trial

Thank you for participating in the BCD (bottles, cups & dummies) trial. This is the final questionnaire. As you may remember our aim is to form a more complete picture of the issues important in breastfeeding premature babies. We would be very grateful if you could answer the following questions as your responses will provide vital information that will help improve the care for women who choose to breastfeed their premature baby. Your responses remain important to us even if you are no longer breast feeding or expressing or if you aren't in the original group you were allocated to. Please return the form via the enclosed prepaid envelope. Thank you for your valuable contribution.

Date: __/__/__

1. Has your baby commenced solids?

Yes ☐ No ☐

↳ **If YES:** How old was your baby when solids were commenced?

.....

2. Please indicate the type of milk, or combination of milks, that your baby has received in the past 24 hours

(please tick one)

breast milk only ☐ *...(go to Q 3)*

breast milk and formula ☐ *...(go to Q 4)*

formula only ☐ *(go to Q 6)*

3. Babies receiving breast milk only (ie no formula)

How many feeds did your baby receive in the last 24 hours? ☐

Of these breast milk feeds how many were:

a) direct Breast feeds? ☐

b) expressed breast milk (EBM) given by bottle? ☐

c) EBM given by cup? ☐

(Now go to Q 8)

4. Babies receiving breast milk and formula

Please tick which statement most closely describes the proportion of breast milk your baby receives:

a) More than half milk feeds are breast milk the rest are formula ☐

b) About half milk feeds are breast milk and half formula ☐

c) Less than half milk feeds are breast milk, the rest are formula ☐

(Now go to Q 5)

5. Babies receiving breast milk and formula.

How many milk feeds did your baby .receive in the last 24 hours? ☐

Of these feeds how many were:

a) direct breast feeds? ☐

b) expressed breast milk (EBM) given by bottle ☐

c) EBM given by cup? ☐

d) formula given by bottle? ☐

e) formula given by cup? ☐

(go to Q 8)

6. If you are not breast feeding your baby, how old was your baby when you stopped breast feeding or expressing?

5 months to less than 6 months ☐

6 months to less than 7 months ☐

7 months to less than 8 months ☐

8 months to less than 9 months ☐

9 months to less than 10 months ☐

10 months to less than 11 months ☐

Other (please specify) ☐

.....

(go to Q 7)

7. What were your reason or reasons for stopping breastfeeding?
(Please tick as many reasons that apply)

I went back to work ☐
It was difficult to express at my workplace (not enough time/facilities) ☐
My baby was fussy during breast feeding ☐
My baby was fussy after breast feeding ☐
I wanted to be able to sleep longer ☐
I had a medical reason ☐
(please specify).....
My baby refused the breast ☐
My baby had a poor weight gain ☐
I had sore nipples ☐
My baby took the bottle better ☐
I didn't feel my milk was good enough ☐
My baby breast fed too frequently ☐
I thought my baby wasn't getting enough ☐
I wanted to make sure my baby got enough ☐
My doctor advised me to stop ☐
I didn't feel I had enough milk anymore ☐
I thought it was time to wean my baby ☐
My baby weaned her/himself ☐
I breast fed my baby for as long as I had planned to ☐
Other *(please specify)* ☐

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8. Did you use a nipple shield when breast feeding your baby?

Yes ☐ No ☐ *(go to Q 9)*

↳ **If YES:** Did you stop using the nipple shield before your baby was **3 months** old?

Yes ☐ *(go to Q 9)*
No ☐

↳ **If NO:** How old was your baby when you stopped using a nipple shield?

3 months to less than 4 months ☐
4 months to less than 5 months ☐
5 months to less than 6 months ☐
Still using a nipple shield ☐
Other (please specify) ☐

.....

9. How much does your baby weigh now?

_____ kg

Date weighed: ...../...../.....

10. Does your baby use a dummy now?

Yes ☐ No ☐

This question relates to your feelings about taking part in the study:

11. If you were in the same situation again, would you participate in such a study?

Yes ☐ No ☐
Maybe ☐

Comment:.....
.....
.....
.....
.....
.....

12. If there is anything else you would like to add, your comments would be much appreciated:

.....
.....
.....
.....
.....
.....

As you have been through a lot in having a premature baby we would also like to know how you are feeling now. Please tick the box of the answer which comes closest to how you have felt IN THE PAST 7 DAYS, not just how you feel today.

Here is an example already completed.

I have felt happy:

Yes, all the time ☐ *No, not very often* ☐

Yes, most of the time ☑ *No, not at all* ☐

This would mean: "I have felt happy most of the time during the past week"

If the results of this part of the questionnaire suggest that you may be depressed would you like to be contacted Yes ☐ **No** ☐

In the past 7 days:

1. I have been able to laugh and see the funny side of things:-

- as much as I always could ☐
- not quite so much now ☐
- definitely not so much now ☐
- not at all ☐

2. I have looked forward with enjoyment to things:-

- as much as I ever did ☐
- rather less than I used to ☐
- definitely less than I used to ☐
- hardly at all ☐

3. I have blamed myself unnecessarily when things went wrong:-

- yes, most of the time ☐
- yes, some of the time ☐
- not very often ☐
- no, never ☐

4. I have been anxious or worried for no good reason:-

- no, not at all ☐
- hardly ever ☐
- yes, sometimes ☐
- yes, very often ☐

5. I have felt scared or panicky for no very good reason:-

- yes, quite a lot ☐
- yes, sometimes ☐
- no, not much ☐
- no, not at all ☐

6. Things have been getting on top of me:-

- yes, most of the time I haven't been able to cope ☐
- yes, sometimes I haven't been coping as well as usual ☐
- no, most of the time I have coped quite well ☐
- no, I have been coping as well as ever ☐

7. I have been so unhappy that I have had difficulty sleeping:-

- yes, most of the time ☐
- yes, quite often ☐
- not very often ☐
- no, not at all ☐

8. I have felt sad or miserable:-

- yes, most of the time ☐
- yes, quite often ☐
- not very often ☐
- no, not at all ☐

(continued next page)

9. I have been so unhappy that I have been crying:-

- yes, most of the time ☐
- yes, quite often ☐
- only occasionally ☐
- no, never ☐

10. The thought of harming myself has occurred to me:-

- yes, quite often ☐
- sometimes ☐
- hardly ever ☐
- never ☐

(EDINBURGH POSTNATAL DEPRESSION SCALE (EPDS)
JL Cox, JM Holden, R Sagovsky)

THANK YOU FOR YOUR TIME AND CONTRIBUTION TO THIS IMPORTANT RESEARCH - YOUR INVOLVEMENT WILL CERTAINLY MAKE A DIFFERENCE TO THE FUTURE CARE OF BREAST FEEDING PREMATURE BABIES.

We will notify you of the results of this research when they are available.

If you require further information or have any queries please do not to hesitate to contact:

Carmel Collins, Research Nurse/Midwife,
Dept. Nursing & Midwifery Research & Practice Development
Women's & Children's Hospital, 72 King William Rd, Nth Adelaide. 5006. Tel: 82047000.

Form No. 3B

Study No: ☐☐☐☐

Database No: ☐☐☐☐

The BCD Trial

Thank you for participating in the BCD (bottles, cups & dummies) trial. This is the final questionnaire. As you may remember our aim is to form a more complete picture of the issues important in breastfeeding premature babies. We would be very grateful if you could answer the following questions as your responses will provide vital information that will help improve the care for women who choose to breastfeed their premature baby. Your responses remain important to us even if you are no longer breast feeding or expressing or if you aren't in the original group you were allocated to. Please return the form via the enclosed prepaid envelope. Thank you for your valuable contribution.

Date: __/__/__

1. Has your baby commenced solids?

Yes ☐ No ☐

If YES: How old was your baby when solids were commenced?

.....

2. How much does your baby weigh now?

_____ kg

Date weighed: ...../...../.....

3. Does your baby use a dummy now?

Yes ☐ No ☐

This question relates to your feelings about taking part in the study:

4. If you were in the same situation again, would you participate in such a study?

Yes ☐ No ☐

Maybe ☐

Comment:.....

.....

.....

.....

.....

.....

5. If there is anything else you would like to add, your comments would be much appreciated:

.....

.....

.....

.....

.....

.....

As you have been through a lot in having a premature baby we would also like to know how you are feeling now. Please tick the box of the answer which comes closest to how you have felt IN THE PAST 7 DAYS, not just how you feel today.

Here is an example already completed.

I have felt happy:

Yes, all the time ☐ *No, not very often* ☐

Yes, most of the time ☑ *No, not at all* ☐

This would mean: "I have felt happy most of the time during the past week"

If the results of this part of the questionnaire suggest that you may be depressed would you like to be contacted Yes ☐ **No** ☐

(continued next page)

In the past 7 days:

1. I have been able to laugh and see the funny side of things:-

- as much as I always could ☐
- not quite so much now ☐
- definitely not so much now ☐
- not at all ☐

2. I have looked forward with enjoyment to things:-

- as much as I ever did ☐
- rather less than I used to ☐
- definitely less than I used to ☐
- hardly at all ☐

3. I have blamed myself unnecessarily when things went wrong:-

- yes, most of the time ☐
- yes, some of the time ☐
- not very often ☐
- no, never ☐

4. I have been anxious or worried for no good reason:-

- no, not at all ☐
- hardly ever ☐
- yes, sometimes ☐
- yes, very often ☐

5. I have felt scared or panicky for no very good reason:-

- yes, quite a lot ☐
- yes, sometimes ☐
- no, not much ☐
- no, not at all ☐

6. Things have been getting on top of me:-

- yes, most of the time I haven't been able to cope ☐
- yes, sometimes I haven't been coping as well as usual ☐
- no, most of the time I have coped quite well ☐
- no, I have been coping as well as ever ☐

7. I have been so unhappy that I have had difficulty sleeping:-

- yes, most of the time ☐
- yes, quite often ☐
- not very often ☐
- no, not at all ☐

8. I have felt sad or miserable:-

- yes, most of the time ☐
- yes, quite often ☐
- not very often ☐
- no, not at all ☐

9. I have been so unhappy that I have been crying:-

- yes, most of the time ☐
- yes, quite often ☐
- only occasionally ☐
- no, never ☐

10. The thought of harming myself has occurred to me:-

- yes, quite often ☐
- sometimes ☐
- hardly ever ☐
- never ☐

(EDINBURGH POSTNATAL DEPRESSION SCALE (EPDS)
JL Cox, JM Holden, R Sagovsky)

THANK YOU FOR YOUR TIME AND CONTRIBUTION TO THIS IMPORTANT RESEARCH - YOUR INVOLVEMENT WILL CERTAINLY MAKE A DIFFERENCE TO THE FUTURE CARE OF BREAST FEEDING PREMATURE BABIES.

We will notify you of the results of this research when they are available.

If you require further information or have any queries please do not to hesitate to contact:
Carmel Collins, Research Nurse/Midwife,
Dept. Nursing & Midwifery Research & Practice Development
Women's & Children's Hospital, 72 King William Rd, Nth Adelaide. 5006. Tel: 82047000.

Do I need to continue in the trial if I change my mind later on?

If you choose to be part of this trial, you can withdraw from the trial at any time without in any way affecting the care of your baby or yourself.

By taking part in this study you will:

- help us answer this important question of the effect that artificial teats (dummy and bottle) have on breast feeding.
- contribute information that will further help us in our understanding of breast feeding premature babies.

THANK YOU FOR CONSIDERING BEING A PART OF THIS IMPORTANT TRIAL

For further information please contact the trial personnel at the Women's & Children's Hospital (listed over) or staff from the Neonatal Intensive Care or Special Care Baby Units.

Trial contact persons:

Ms. Carmel Collins

Research Nurse/Midwife
Dept. Nursing & Midwifery Research
& Practice Development
☎: 82047000.

Dr. Andy McPhee

Medical Head
Neonatal Intensive Care Unit.
☎: 82047000.

Dr Caroline Crowther

Senior Lecturer
Dept. Obstetrics & Gynaecology
☎: 82047000

THE BCD TRIAL

(BOTTLES, CUPS & DUMMIES)

PARENT INFORMATION SHEET.

Premature babies start having their milk feeds by a small tube into their stomach. The change from tube to breast feeds gradually happens over a number of weeks. You start by having regular (every one to two days) skin-to-skin contact with your baby and putting him/her to the breast. Gradually your baby will mature into being able to breast feed once a day. This happens around 33 weeks gestation. Breast feeds increase as your baby matures, tube feeds continue until your baby can manage all breast feeds.

The reason we are doing this trial is because debate has arisen about whether artificial teats (bottle or dummy) interfere with establishing breast feeds. There is no scientific data to support this theory, although there is a difference in the sucking action required for an artificial teat and the breast. There has also been recent evidence from England that suggests that giving your baby milk with a small cup may increase the success in breast feeding.

The studies that have been done on the use of dummies in preterm babies showed that if the baby sucked a dummy during the tube feed, the number of days to the first *bottle* feed was reduced by 3 days, and the number of days to go from all tube feeds to all bottle feeds was also reduced. These studies looked at the effect on bottle feeding; the effect on breast feeding is not known.

Our practice currently is to give your breast milk by a bottle when you are unable to be there to breast feed, or if your baby requires a "top-up" after a breast feed. We also give dummies to all babies. It is very important for this trial to be undertaken as there has not been any done that look at the premature baby's transition to breast feeds.

This trial has been approved by the Women's and Children's Research and Ethics Committee. To meet the criteria of this committee you will be asked to sign a consent form if you choose to be part of the trial.

What is the study about?

The study is designed to see which strategy of care for your baby, in their transition to breast feeds, is the best for successful breast feeding (bottles or cups with or without dummies).

You are eligible to enter the trial if:

Your baby is less than 34 weeks gestation and you wish to breast feed your baby.

How will the trial be done?

Parents and their babies agreeing to take part in the trial will be randomly divided into two groups (neither you nor the staff will be able to choose which group).

One group will receive dummies the other group won't. Further randomisation will then occur - one group will use bottles for those times when they are unable to be there to breast feed or if the baby needs a "top-up" after a breast feed. The other group will use cups.

You therefore could be in one of the following four groups:

- Breast, no dummy and cup,
- Breast, no dummy and bottle,
- Breast, dummy and cup,
- Breast, dummy and bottle.

Whichever group you are in the midwifery and nursing staff will teach you how to do it.

A questionnaire will be sent to you at 3 and 6 months after discharge home.

Benefits or risks?

Cup feeding and bottle feeding are both safe ways of supplementing your baby's breast feeds. For the babies that are in the no dummy group, non nutritive sucking can still occur by putting your baby to the breast. There are many ways of pacifying babies, which include containing, allowing them to put their hands to their mouth, rocking, and holding. The staff will show you how to do this.

Appendix IX: Trial entry form

The BCD Trial **TRIAL ENTRY FORM**

Date: ☐☐ ☐☐ ☐☐
(day) (month) (year)

Patient sticker

Baby's first name: .....

Mothers name: ....
(surname) *(first)*

Fathers name: ....
(surname) *(first)*

☎: (.....).....

INCLUSION CRITERIA:

Gestation: ____ weeks
Must be less than 34 weeks *(any gestation up to 33⁶)*

Wishes to breast feed: ____ **(Must be YES)**

EXCLUSION CRITERIA:

Congenital abnormality precluding enteral feeds (eg T.O.F) ____ **Must be NO**

Has the baby had a:
cup ____ **Must be NO**
bottle ____ **Must be NO**
dummy ____ **If Yes →,**
dummy ≤ 48 hrs ____ Must be **YES**

CONSENT: ☐ **yes** ☐ **no**

If YES: Consent form signed: ☐
Telephone Rose ward (Ext.7253) for randomisation.

If **NO:** please give reason:
.....
.....
.....

(If does not wish to participate in the study do not complete below)

STUDY NUMBER AT RANDOMISATION: ☐ ☐ ☐ ☐

CHECK: Gestation <28 weeks, study number begins with 1, Gestation 28-<34 weeks, study number begins with 2.

Date randomised: ...../...../..... Time randomised .....

STUDY GROUP ALLOCATED:

Dummy ☐ **Bottle** ☐
No dummy ☐ **Cup** ☐

(Address of parents, in-laws or other permanent contacts, in case of moving)

Name: .... Relationship: .....

Address: ..... ☎ (.....).....
.....
.....

Database record No. ☐☐☐☐
(Researcher to enter)

For any queries please contact:
Carmel Collins, Research Nurse/Midwife
Pager 18004.

Appendix X: Post-randomisation exclusion characteristics

Table X.1 Post-randomisation exclusions - maternal characteristics

Characteristic (Total No. respondents in each group).	Cup/ No Dummy (n=7)	Cup/ Dummy (n=3)	Bottle/ No Dummy (n=3)	Bottle/ Dummy (n=3)
	n	n	n	n
Parity (n=7/3/2/3)				
Primiparous	4	1	1	1
Multiparous	3	2	1	2
Maternal age (n=7/3/2/3)				
<25 years	1	2	0	1
25-34 years	4	1	2	2
≥35 years	2	0	0	0
Lives with another adult (n=3/2/3/2)	3	2	2	2
Education (n=5/3/3/3)				
Incomplete High School	1	1	2	2
Complete High School	1	1	1	1
Tertiary	3	1	0	0
Main income source (n=3/2/3/3)				
Part time work	0	0	0	0
Full time work	2	1	1	2
Benefits	1	1	2	1

Table X.2 Post-randomisation exclusions - breast feeding experience

Breast feeding (Total No. respondents in each group).	Cup/No Dummy (n=7)	Cup/ Dummy (n=3)	Bottle/ No Dummy (3)	Bottle/ Dummy (n=3)
	n	n	n	n
During pregnancy had planned to breast feed (n=3/2/3/3)	3	2	3	3
Length of time planned to breast feed (n=3/2/3/3)				
≤ 6 weeks	0	0	0	0
>6 weeks to ≤ 3 months	1	0	0	0
>3 months to ≤ 6 months	0	0	1	0
> 6 months	2	1	1	3
Don't know	0	1	1	0
Breast fed before (n=3/3/3/3)				
Yes	1	1	1	2
No	2	2	2	1
Length of time breast fed before (n=3/3/3/3)				
Never	2	2	2	1
≤ 6 weeks	0	1	0	0
>6 weeks to ≤ 3 months	1	0	0	0
>3 months to ≤ 6 months	0	0	0	0
> 6 months	0	0	1	0

Table X.3 Post-randomisation exclusions - birth characteristics

Characteristic (Total No. respondents in each group).	**Cup/ No Dummy (n=7)**	**Cup/ Dummy (n=3)**	**Bottle/ No Dummy (n=3)**	**Bottle/ Dummy (n=3)**
	n	n	n	n
Hospital recruited to (n=7/3/3/3)				
WCH	3	0	1	0
MHW	4	3	2	3
Twins	2	1	0	0
Method of delivery (n=7/3/2/3):				
Vaginal	4	1	0	1
Instrument	1	0	0	0
Caesarean, no labour	0	0	0	0
Caesarean with labour	2	2	2	2
*Birth weight, grams (n=7/3/2/3)	1049±440 (552 to 1700)	825±253 (609 to 1104)	761±58 (720 and 802)	691±55 (638 to 748)
Gestational age at birth: (n=7/3/3/3)				
<28 weeks	4	1	1	3
28 to ≤ 34 weeks	3	2	2	0

*Mean±SD (Range)

Appendix XI: Outcomes by recruiting hospital

XI.I Breast feeding on discharge home by recruiting hospital

XI.I.I No Dummy versus Dummy

More infants were recruited from the MHW, they comprised 67% (n=101) of the No Dummy group and 65% (n=98) of the Dummy group. Breast feeding outcomes were similar between recruiting hospitals as shown in Table XI.1.

Table XI.1 Breast feeding status on discharge home, by hospital

Breast feeding status	**WCH (n=104)**	**MHW (n=199)**
	n (%)	n (%)
Any breast feeding	70 (67)	145 (73)
Fully	*55 (53)*	*109 (55)*
Partially	*15 (14)*	*36 (18)*
Not breast feeding	34 (33)	54 (27)

Table XI.2 shows the breast feeding status on discharge home by recruiting hospital and dummy allocation. A similar proportion of infants, by dummy allocation, were discharged home with any breast feeding from both recruiting hospitals. Of infants recruited from the WCH, a higher proportion were discharged home fully breast feeding if randomised to No Dummy compared to those randomised to Dummy. In contrast, infants recruited from the MHW had a higher proportion of infants discharged home fully breast feeding who were randomised to the Dummy group.

Table XI.2 Breast feeding status by recruiting hospital and dummy allocation

	WCH		**MHW**	
Breast feeding status	**No Dummy (n=51)**	**Dummy (n=53)**	**No Dummy (n=101)**	**Dummy (n=98)**
	n (%)	n (%)	n (%)	n (%)
Any breast feeding	34 (67)	36 (68)	73 (72)	72 (74)
Fully	*29 (57)*	*26 (49)*	*50 (50)*	*59 (60)*
Partially	*5 (10)*	*10 (19)*	*23 (23)*	*13 (13)*
Not breast feeding	17 (33)	17 (32)	28 (28)	26 (27)

* Percentages may not sum to 100 due to rounding

XI.1.2 Cup versus Bottle

More infants were recruited from the MHW, they comprised 64% (n=96) of the Cup group and 68% (n=103) of the Bottle group.

Table XI.3 shows the breast feeding status on discharge home by recruiting hospital and Cup versus Bottle allocation. Infants recruited from the WCH and randomised to the Cup groups had a higher proportion of any breast feeding on discharge home than infants randomised to the Bottle groups. In contrast, infants recruited from the MHW had a similar prevalence of any breast feeding in both Cup and Bottle groups. For the outcome fully breast feeding infants, from both recruiting hospitals had a higher prevalence if randomised to the Cup groups.

Table XI.3 Breast feeding status by recruiting hospital and Cup versus Bottle*

	WCH		MHW	
Breast feeding status	**Cup (n=55)**	**Bottle (n=49)**	**Cup (n=103)**	**Bottle (n=96)**
	n (%)	n (%)	n (%)	n (%)
Any breast feeding	41 (75)	29 (59)	74 (72)	71 (74)
Fully	*34 (62)*	*21 (43)*	*58 (60)*	*51 (50)*
Partially	*7 (13)*	*8 (16)*	*13 (14)*	*23 (22)*
Not breast feeding	14 (26)	20 (41)	25 (26)	29 (28)

* Percentages may not sum to 100 due to rounding

XI.2 Days to all sucking feeds

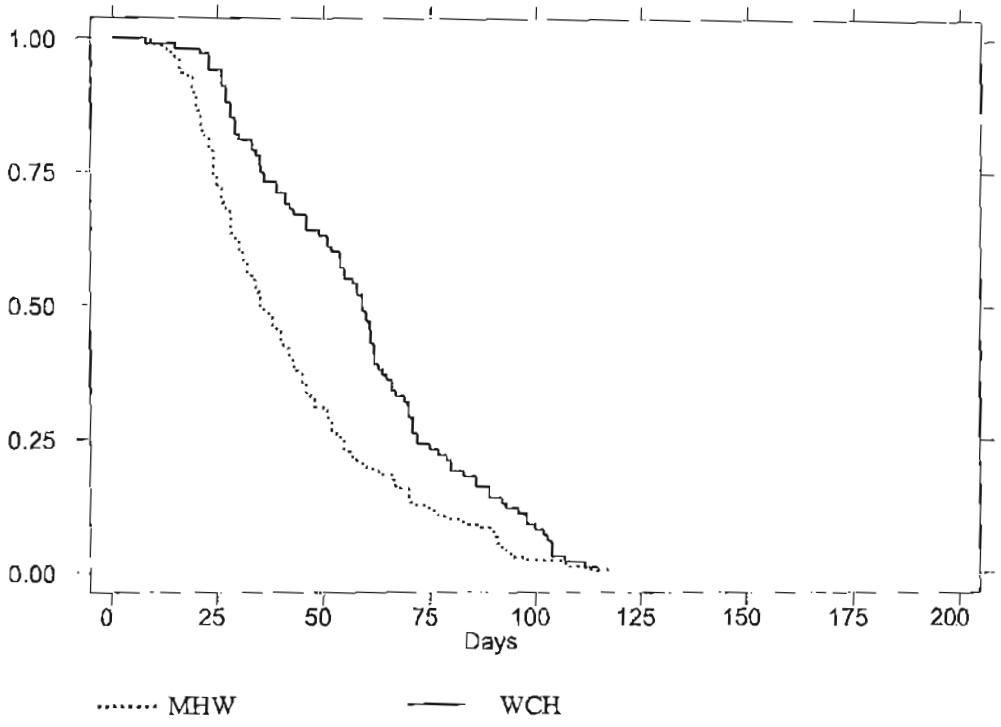
XI.2.1 No dummy versus dummy

More infants included in the survival analysis (n=306) were recruited from the MHW, they comprised 66% (n=105) of the No Dummy group and 67% (n=98) of the Dummy group. Infants recruited from the WCH took significantly longer to reach all sucking feeds compared to infants recruited from the MHW (HR 1.68, 95% CI 1.30 to 2.18, P<0.001) as shown in Table XI.4 and Figure XI.1.

Table XI.4 Days to all sucking feeds by hospital recruited to

Days to all sucking feed	**WCH (n=103)**	**MHW (n=203)**
Median (days)	59	35
Interquartile range	36-72	24-54

Figure XI.1 Kaplan-Meier survival estimates days to all sucking feeds, by recruiting hospital



34% (n=35) of the infants recruited to the WCH and included in this survival analysis were less than 28 weeks gestational age at birth compared to 17% (n=34) of the infants recruited to the MHW. Days to all sucking feeds by gestational age at birth and hospital are presented in Table XI.5 and Table XI.6.

Table XI.5 Days to all sucking feeds – WCH

Gestation (number)	No Dummy	Dummy	No Dummy & Dummy
< 28 weeks (18/17/35)	89 (75-98)	79 (69-102)	86 (70-100)
28 - <34 weeks (37/31/68)	46 (29-55)	42 (29-61)	43 (29-59)

Median (interquartile range)

Table XI.6 Days to all sucking feeds – MHW

Gestation (number)	No Dummy	Dummy	No Dummy & Dummy
< 28 weeks (19/15/34)	76 (66-95)	82 (74-91)	79 (67-93)
28 - <34 weeks (86/83/169)	31 (24-46)	33 (22-45)	32 (24-45)

Median (interquartile range)

Infants recruited at the WCH took longer to reach all sucking feeds compared to infants recruited at the MHW in both gestational age categories. For infants less than 28 weeks gestation at birth those recruited from the WCH took longer to reach all sucking feeds if randomised to No Dummy; in contrast, infants recruited from the MHW had a shorter time

to full sucking feeds if randomised to No Dummy. The more mature infants in each recruiting hospital took a similar length of time to reach all sucking feeds regardless of dummy allocation.

XI.2.2 Cup versus Bottle

More infants included in the survival analysis (n=306) were recruited from the MHW, they comprised 64% of the Cup group (n=101) and 69% of the Bottle group (n=102). Infants recruited from the WCH took significantly longer to reach all sucking feeds, than infants recruited to the MHW as shown in Table XI.4 and Figure XI.1.

34% (n=35) of infants included in the survival analysis and recruited to the WCH were less than 28 weeks gestational age at birth compared with 17% (n=34) of the infants recruited to the MHW. Days to all sucking feeds by gestational age at birth, hospital and Cup or Bottle allocation are presented in Table XI.7 and Table XI.8.

Table XI.7 Days to all sucking feeds – WCH

Gestation (number)	Cup	Bottle	Bottle & Cup
< 28 weeks (18/17/35)	96 (72-104)	77 (67-92)	86 (70-100)
28 - <34 weeks (38/30/68)	46 (30-61)	39 (28-57)	43 (29-59)

Median (interquartile range)

Table XI.8 Days to all sucking feeds – MHW

Gestation (number)	Cup	Bottle	Bottle & Cup
< 28 weeks (21/13/34)	79 (70-93)	77 (67-91)	79 (67-91)
28 - <34 weeks (80/89/169)	35 (24-55)	28 (23-42)	32 (24-45)

Median (interquartile range)

Irrespective of gestational age, infants recruited from the WCH took longer to reach all sucking feeds compared to infants recruited from the MHW.

There was no statistically significant difference in the number of days to all sucking feeds between Cup or Bottle for infants recruited from the WCH (HR 1.39, 95% CI 0.92 to 2.10, P=0.12). The Kaplan-Meier survival curves for infants recruited to the WCH are shown in Figure XI.2 and summary statistics in Table XI.9.

Figure XI.2 Kaplan-Meier survival estimates days to all sucking feeds, by Cup or Bottle allocation, for infants recruited to the WCH

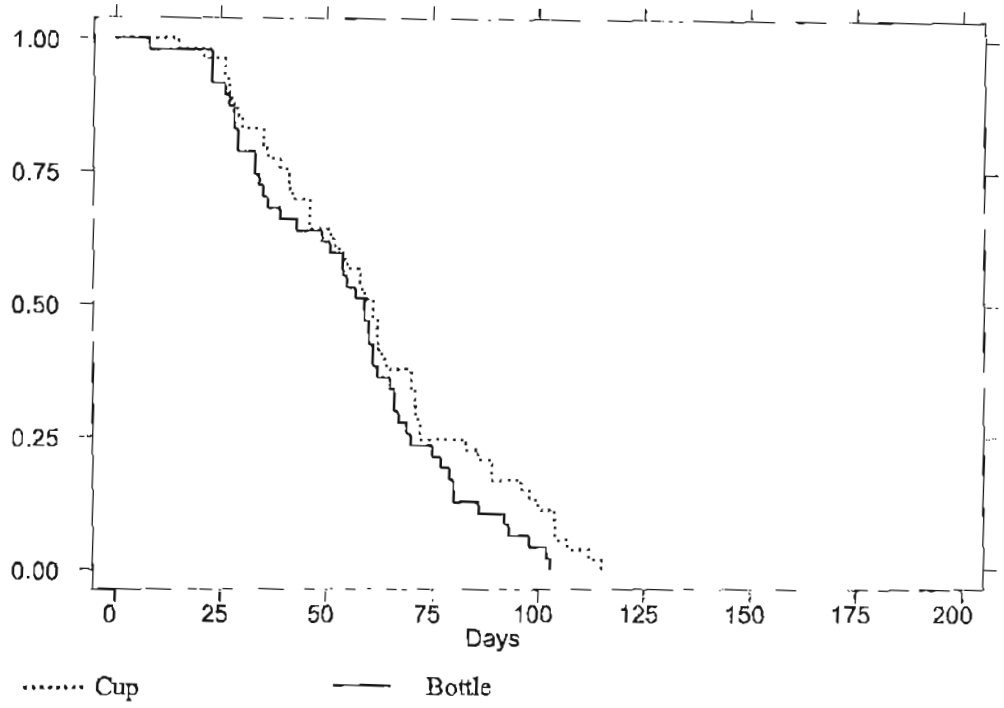


Table XI.9 Days to all sucking feeds by Cup or Bottle allocation and recruited to WCH

Days to all sucking feed	Cup (n=56)	Bottle (n=47)
Median (days)	61	59
Interquartile range	41-72	33-70

There was minimal difference between those randomised to Cup and those to Bottle in the time taken to reach all sucking feeds for infants recruited to the WCH. Compliance for these infants was poorer than that for the MHW, which may explain this disparity. 66% of infants recruited to the WCH and randomised to Cup feeds had a bottle introduced compared with 51% of infants recruited to the MHW.

There was a statistically significant increase in the number of days to all sucking feeds for infants recruited from the MWH and randomised to the cup feeds (HR 1.61, 95% CI 1.14 to 2.27, P=0.01). The Kaplan-Meier survival curves for infants recruited to the MHW are shown in Figure XI.3 and summary statistics in Table XI.10.

Figure XI.3 Kaplan-Meier survival estimates days to all sucking feeds, by Cup or Bottle allocation, for infants recruited to the MHW

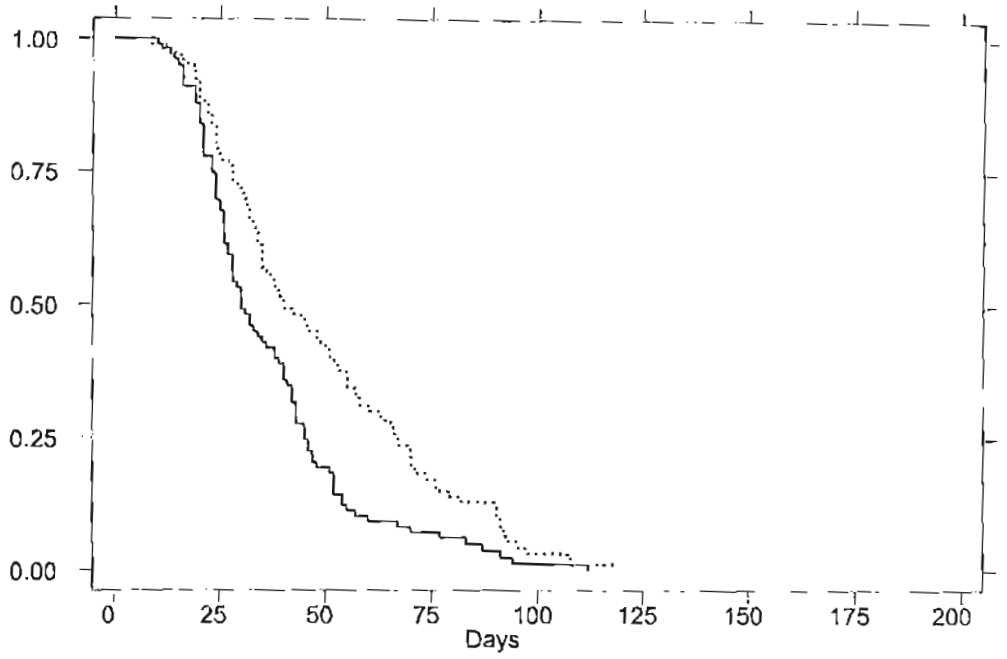


Table XI.10 Days to all sucking feeds by Cup or Bottle allocation and recruited to MHW

Days to all sucking feed	Cup (n=101)	Bottle (n=102)
Median (days)	40	30
Interquartile range	28-67	23-45

XI.3 Length of hospital stay

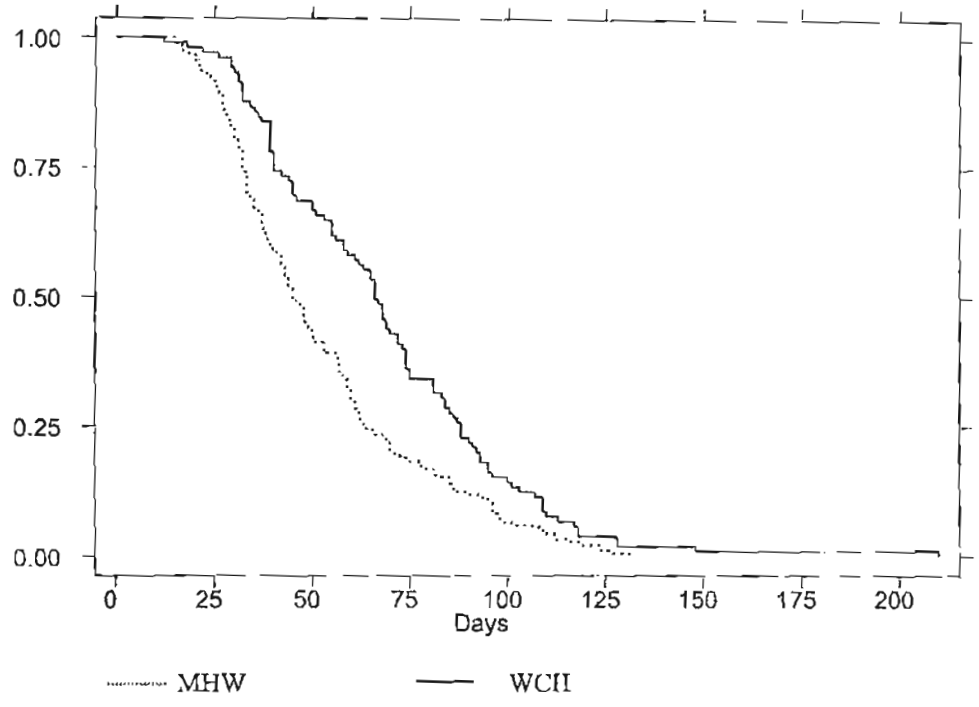
XI.3.1 Cup versus Bottle

More infants were recruited from the MHW, they comprised 64% of the Cup group (n=103) and 68% of the Bottle group (n=108). Infants recruited from the WCH were hospitalised for significantly longer than infants recruited to the MHW (HR 1.60, 95% CI 1.24 to 2.06, P<0.001) and as shown in Table XI.11 and Figure XI.3.

Table XI.11 Duration of hospitalisation by recruiting hospital

Percentile	WCH (n=108) days	MHW (n=211) days
Median	66	45
Interquartile range	40-88	32-64

Figure XI.4 Kaplan-Meier survival estimates duration of hospitalisation, by recruiting hospital



33% (n=36) of the infants included in the survival analysis (n=319) and recruited to the WCH were less than 28 weeks gestational age at birth compared with 19% (n=40) of the infants recruited to the MHW. Duration of hospitalisation by gestational age at birth and hospital are presented in Table XI.12 and Table XI.13.

Table XI.12 Duration of hospitalisation by gestation - WCH

Gestation (number infants)	Cup	Bottle	Total
< 28 weeks (19/17/36)	95 (90-117)	87 (81-100)	93 (85-109)
28 - <34 weeks (39/33/72)	55 (39-70)	44 (39-65)	50 (39-67)

Median (interquartile range)

Table XI.13 Duration of hospitalisation by gestation – MHW

Gestation (number infants)	Cup	Bottle	Total
< 28 weeks (23/17/40)	87 (85-109)	96 (72-98)	90 (81-102)
28 - <34 weeks (80/91/171)	43 (31-62)	38 (31-50)	42 (31-57)

Median (interquartile range)

The length of stay for infants less than 28 weeks gestation at birth who were randomised to Cup feeds was greater than those randomised to Bottle feeds if recruited to the WCH. This was reversed if recruited to the MHW. However, the small numbers in this gestational range preclude much importance being placed on this outcome. Infants 28 weeks or greater at birth had a longer length of hospital stay if randomised to Cup feeds in both recruiting centres.

Figure XI.5 shows the Kaplan-Meier survival curves and Table XI.14 the summary statistics for infants randomised to Cup or Bottle and recruited from the WCH. There was a non significant increase in length of stay for infants randomised to Cup (HR 1.33, 95% CI 0.87 to 2.03, P=0.19).

Figure XI.5 Kaplan-Meier survival estimates duration of hospitalisation - Cup versus Bottle for infants recruited from the WCH

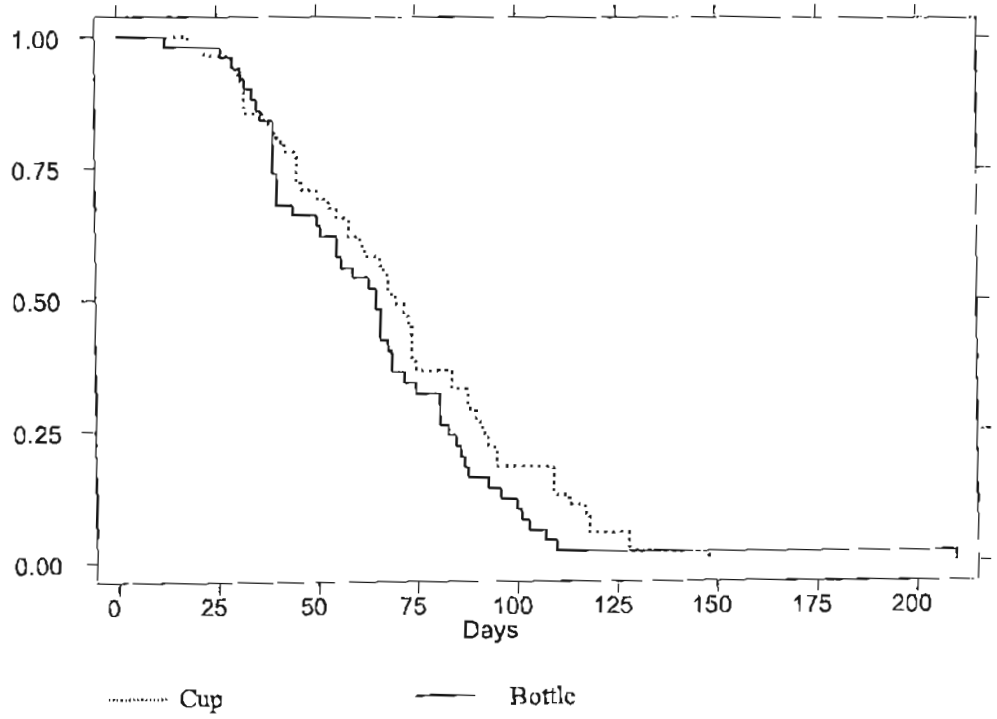


Table XI.14 Duration of hospitalisation – Cup versus Bottle, WCH

Percentile	Cup (n=58)	Bottle (n=50)
	days	days
Median	70	65
Interquartile range	45-90	39-83

Figure XI.6 shows the Kaplan-Meier survival curves and Table XI.15 the summary statistics for infants randomised to Cup or Bottle and recruited from the MHW. There was a significant increase in length of hospital stay for infants randomised to Cup feeds (HR 1.49, 95% CI 1.09 to 2.04, P=0.01).

Figure XI.6 Kaplan-Meier survival estimates duration of hospitalisation – Cup versus Bottle for infants recruited from the MHW

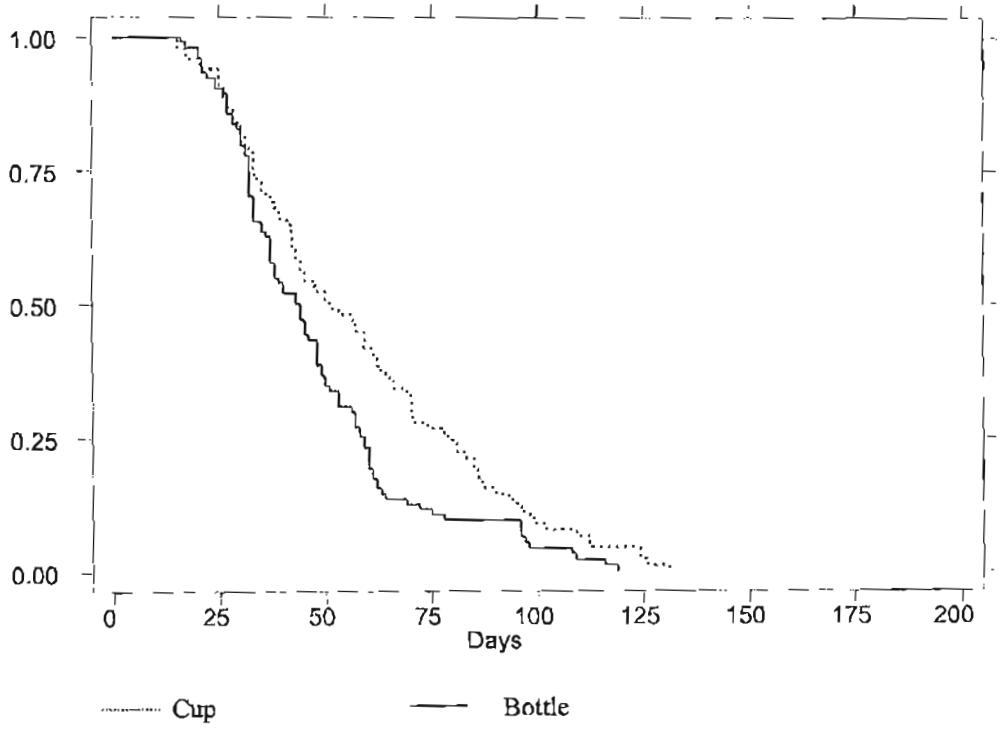


Table XI.15 Duration of hospitalisation – Cup versus Bottle, MHW

Percentile	Cup (n=103)	Bottle (n=108)
	days	days
Median	51	44
Interquartile range	33-79	32-59