NHS Research & Development

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Appendix 2

Breastfeeding promotion in special care baby units and neonatal intensive care units (SCBU/NICU):

an evidence synthesis

Protocol

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Final Version

Contents

1. Review Team (in alphabetical order)

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2. Aims and objectives

The aims of this study are to:

a) evaluate the effects (positive and negative) of interventions that specifically aim to influence breastfeeding/feeding with breast milk for babies who need special care (e.g. in special care baby units (SCBU) and neonatal intensive care units (NICU).

b) assess their cost-effectiveness

c) identify a research agenda

The objectives are:

- to identify, present and synthesise all studies in the literature that examine interventions that aim to affect breastfeeding/ feeding with breast milk in SCBU/NICUs using systematic review (SR) methodology
- to assess their cost-effectiveness through the development of a decision analytical model
- to collate expert opinion on best practice, using the views of Advisory Group members and information from SCBU/NICU settings nationally and internationally where breastfeeding/breast milk feeding rates are high
- based on the formal review and expert opinion, to identify an agenda for future research that will inform key gaps in knowledge

3. Background

3.1. Infant feeding and health

Breastfeeding reduces babies' risk of ill health, particularly gastroenteritis and respiratory infection (eg Quigley et al., 2005), and favourably affects other long term outcomes in both the baby and the mother (eg Beral, 2002). For preterm, growth restricted and sick neonates (including those requiring surgery), breast milk, sometimes fortified depending on the nutritional status of the baby, is the food of choice (Spatz, 2006, Yu, 2005, Canadian Medical Association, 1995). Epidemiological studies (Furman et al., 2003, El-Mohandes et al., 1997) and quasi-randomised controlled trials (Narayanan et

al., 1982) in high-risk environments suggest that the incidence of invasive infection is higher in low birthweight babies fed formula. A recent meta-analysis of randomised controlled trials has shown that formula-fed low birth weight babies are at five times the risk of necrotising enterocolitis (NEC)(Boyd et al., 2006), a condition associated with a mortality of approximately 20% and significant long-term healthcare costs amongst survivors (Bisquera et al., 2002). In a UK randomised controlled trial breastmilk feeding achieved earlier transition from parenteral nutrition (Lucas and Cole, 1990), reducing the associated cost and infection risk. Compared with bottle feeding, breastfeeding is associated with less thermal and cardiovascular stress in low birthweight babies (Meier, 1988, Chen et al., 2000), supporting the encouragement of early feeding from the breast. This may facilitate other beneficial outcomes, for example a reduction in procedural pain (Shah et al., 2006, Carbajal et al., 2003), and earlier discharge (Callen et al., 2005, Johnson et al., 1999), and it has been argued that supporting mothers in breastfeeding and providing breast milk is an essential part of a package of humane care, and assists in promoting attachment (Chalmers and Levin, 2001). Follow-up data from prospective studies show that babies fed on human milk have an IQ advantage of approximately 4-8 points after adjustment of identifiable confounders (Anderson et al., 1999, Vohr et al., 2006). This may be particularly important in the context of a population at increased risk of impairment. They also exhibit a more favourable cardiovascular risk profile in terms of systolic blood pressure (Singhal et al., 2001) and glucose tolerance (Singhal et al., 2003). After discharge from hospital low birthweight babies, a group at increased risk of hospital readmission, are exposed to fewer of the hazards associated with infant feeding if breastfed. These include contamination of feeds and errors of reconstitution (Department of Health, 2006, Renfrew et al., 2003, World Health Organisation, 2005).

3.2. Breastfeeding in the UK

Breastfeeding initiation rates in the UK are among the lowest in Europe; only 43% of women were still breastfeeding at all at six weeks after birth in the 2000 national survey (Hamlyn et al., 2002). The breastfeeding initiation rates in the countries making up the UK in 2005 were 78% in England, 70% in Scotland, 67% in Wales and 63% in Northern Ireland (Bolling et al 2007). The rate of women breastfeeding at all at 6 weeks after birth in the 2005 national survey had increased to 48% (50% in England, 37% in Wales (49% in England & Wales), 44% in Scotland and 32% in Northern Ireland). Exclusive breastfeeding rates are also very low; in 2000 only a quarter of those breastfeeding were breastfed exclusively at two months (in 2005 this rate was 27% for UK overall, Bolling et al 2007 table 2.33), and one sixth at three to five months (in 2005, 21% at 3 months and 5% at 5 months for UK overall, Bolling et al 2007 table 2.33). Incidence and prevalence are lowest among families from lower socio-economic groups (Bolling et al 2007 tables 2.4 and 2.12), particularly among white women compared to those of Asian, black or mixed ethnicity (Griffiths et al., 2005), Bolling et al 2007 tables 2.7 and 2.15). Teenage, young mothers and those least educated are also vulnerable groups, being half as likely as older mothers to initiate any breastfeeding.

Bolling et al 2007 (table 2.6): incidence of breastfeeding by mother's age and country in 2000 and 2005:

% who breastfed initially in United Kingdom:

	20 or under	20-24	25-29	30-34	35 or over	All mothers
2000	46	58	67	76	80	69
2005	51	67	76	83	84	76

Table 2.13 gives breastfeeding at birth in 2005 by age mother left full time education:

16 or under (61%), 17 or 18 (73%), over 18 (90%), all mothers (76%).

As there is an over-representation of babies born to women from these backgrounds in SCBU/NICU (Macfarlane and Mugford, 2000), mothers of babies born too small or too soon will have real challenges in continuing to breastfeed even if they are encouraged to start. Eight per cent of babies in The Infant Feeding Survey 2005 (Bolling et al 2007) were admitted to special care. No difference in initiation of breastfeeding by whether baby started life in special care was found. However, babies starting life in special care were slightly more likely to be breastfed both at one week (68% of special care babies compared with 64% of other babies) and at two weeks (63% compared with 60%). The differential increased with length of time spent in special care, with 73% of babies spending at least four days in special care being breastfed at one week compared with 61% of babies only spending a day and 64% not in special care at all. Similarly the prevalence of breastfeeding at two weeks increases from 58% of babies spending up to a day in special care to 67% spending four or more days.

Reasons for the low prevalence of breastfeeding in the UK include the influence of societal and cultural norms, poor continuity of care in the health services, and a lack of effective care by health professionals in hospital and community (Smale et al., 2006). These factors are likely to be amplified in SCBU/NICU settings, making continuation of breastfeeding/breastmilk feeding difficult for those who do start. A recent study has found that paediatricians and GPs are particularly ill-prepared to promote and support breastfeeding (Wallace and Kosmala-Anderson MCN 2006), yet SCBU/NICUs are often dominated by a medical ethos and procedures. The atmosphere in a SCBU/NICU, described as 'stressful', 'frightening', and 'difficult' by American mothers (Bernaix et al., 2006), is not conducive to breastfeeding or breast milk expression. Additionally mothers are more likely to have experienced a complicated labour and/or birth, to be prescribed medication, and to be anxious about their children's wellbeing and even survival. In spite of these complex problems, there are examples internationally and in the UK of

SCBU/NICU settings where the prevalence of breastfeeding or use of human milk is very high, even in low income populations (eg Porteous et al, 2000), demonstrating that high rates can be achieved and sustained.

Despite strong policy support for breastfeeding initiation and duration in recent years in the UK (eg (Department of Health, 2003)), there has never been a UK policy initiative specifically intended to increase breastfeeding uptake in SCBU/NICUs, and few UK studies supporting breastfeeding in these families have been conducted.

3.3. Costs of infant feeding

Studies have demonstrated increased costs resulting from artificial feeding in terms of the burden of ill health placed on health services (Hoey and Ware, 1997, Riordan, 1997, Ball and Wright, 1999). A recent unpublished rapid review of ours identified very few cost effectiveness studies specifically relevant to feeding in SCBU/NICU settings, however (McCracken et al pers comm). Both the direct costs associated with infant feeding (eg service provision), and the indirect costs (eg impact on clinical outcomes and related service costs plus those arising from parental income lost through childhood illness and long term population health impact) are important.

4. Review questions

The main research questions for this review are:

- What are the effects (positive and negative) of interventions that aim to affect breastfeeding/feeding with breast milk for babies who need special care (i.e. in SCBU/NICU settings)?
- What is their cost-effectiveness (in terms of increased duration and health benefit to the infant)?

In order to manage this broad scope, this review will identify and synthesise intervention studies that address the following sub-questions.

1. What are the most effective (and potentially harmful) interventions to deliver breast milk to babies needing special care?
2. Does pacifier use (with or without breastmilk to taste) or non-nutritive sucking affect their breastfeeding behaviour?
3. What interventions demonstrate how breast milk composition may be adjusted (e.g. using creamatocrits) to meet the nutritional needs of small/sick babies?
4. What type of mother and baby contact effectively encourages/facilitates breastfeeding/ feeding with breast milk (e.g. skin to skin, kangaroo care, helping with other forms of feeding, positioning baby for feeding – eg upright)?
5. Do interventions that increase access to and involvement of mother/family with the baby in special care affect breastfeeding or feeding with breast milk?

6. What education and/or support interventions for mothers/families of babies needing special care may effectively promote breastfeeding/feeding with breast milk?
7. What organisational structures effectively facilitate breastfeeding/feeding with breast milk for babies needing special care?
8. What interventions promote breast milk expression in mothers of babies needing special care?
9. What types of staff training effectively support feeding with breastmilk, and breastfeeding for babies who need special care?

5. Participants, interventions and outcomes of interest

5.1. Participants

Participants of interest in this review include:

- Babies who are not both term and healthy and who therefore require special care (e.g. in NICU or SCBUs). The babies include preterm, growth restricted and sick neonates, multiples, babies requiring surgery and babies with feeding problems, hypoglycaemia and jaundice.

Breastfeeding is an activity that involves the mother as much as the baby and which needs support from family, carers and others. Questions 4, 5 and 6 will also include mothers and families of babies requiring special care. For questions 8 and 9, the participants will include either:

- Mothers of babies in special care, excluding mothers not able to express breast milk (too ill, medical/ post surgical condition, living far away)
- Healthcare staff working with babies in SCBU/NICUs which may include midwives, nurses, nursery nurses, consultants, paediatricians, breastfeeding counsellors, lactation consultants, and others

5.2. Interventions

As presented above, interventions that specifically address breastfeeding/feeding with breast milk in SCBU/NICUs will be included in the review. A list of interventions of interest is presented in Table 1. Studies which examine the effectiveness of breast milk on clinical outcomes (e.g. studies that examine associations between breast milk consumption and the incidence of necrotising enterocolitis) will not be reviewed, but will be included in the background section of the review. In addition, studies that evaluate the nutritional content of formula and breast milk fortifiers; or the establishment and maintenance of milk banking will not be included in the review (although studies that examine the availability of a milk bank/donor milk will be included).

5.3. Outcomes

To be included in the review, a study must report a breastfeeding/breast milk related outcome. These may include breast milk composition and volume, licking mothers' nipple/ tasting dripped breast milk, number of sucks, initiation

of breastfeeding, any breastfeeding, exclusive breastfeeding, and rates of breastfeeding at discharge and beyond.

Secondary outcomes of interest may include clinical/health outcomes (e.g. necrotising enterocolitis, gastrointestinal disease, weight), process outcomes (e.g. time of hospital discharge, readmission, time spent by mother in contact with baby), psycho-social outcomes (e.g. views of mothers, fathers, families, health care staff) (see Table 1) and cost-effectiveness outcomes.

Outcomes will be assessed for the different gestational ages of the baby and/or ability to coordinate sucking and swallowing – for example, as the practice and outcomes for skin-to-skin care will be different for extremely low birthweight babies when compared with low birth weight babies, and for babies with specific neurological problems.

Table 1 Participants, interventions and outcomes of interest

Participants	**Interventions**	**Primary outcomes**	**Secondary outcomes**
Babies who need special care (eg in. NICU, SCBU)	***Interventions to deliver breast milk to babies:*** •Methods of feeding (tube, cup, spoon, supplementer, bottle, nipple shields)	•Proportion of babies' nutritional needs met by breast milk •Effective delivery of breast milk in babies with different abilities/needs •Any behaviour at breast pre full breastfeeding (e.g. licking, tasting dripped breast milk, some sucking) •Any/exclusive breastfeeding at any time before, or after discharge	•Clinical/health outcomes •Weight gain •Time taken for feeds •Time spent by mother in contact with baby •Views of mother, family and staff •Length of stay •Readmission •Costs
	Interventions that may affect breastfeeding behaviour: •Pacifiers (or non-nutritive sucking): with and without use of breastmilk to taste •Timing feeds according to cues/baby's state		
	Interventions to support adequate nutritional intake (e.g. fat, protein) from breast milk: •Creamatocrits •Hind milk vs fore milk •Morning expression vs later expression		

	Interventions involving physical contact: •Skin-to-skin contact (mother and father) •Kangaroo mother contact		
	Interventions involving access to and caring for the baby: •Enabling mother to stay with and/or care for the baby (including rooming in or 24 hr visitation) •Involving family in aspects of baby care including feeding by tube/cup etc		
	Interventions involving breastfeeding education and/or support: •Breastfeeding education to parents and families •Breastfeeding support by the fathers/families •Support from peers and/or professionals (antenatally and postnatally)		

	Interventions involving other aspects of organisation of care: •Facilities for expression and storage •Availability of milk bank/donor milk (not running of a milk bank) •Feeding policies •Policies for handling and testing breast milk •Early discharge •Staffing levels and organisation		
Mothers of babies who need special care	***Interventions that affect breast milk expression:*** •Methods of breast milk expression •Teaching and support of breast expression •Galactagogues	•Ease of breast milk expression •Quantity/quality of breast milk expressed •Ever breastfed •Any/exclusive breastfeeding at discharge and any point afterwards	•Time spent by mother in contact with baby •Views of mothers, family and staff •Costs
Health care staff looking after babies who need special care	***Interventions involving staff training:*** •Staff training in breastfeeding support and in prescribing of drugs for breastfeeding women •Staff training in baby weight gain	•Skills of staff as measured by breastfeeding/milk feeding outcomes	•Hospital discharge, i.e. if staff less worried about weight of breastfeeding baby •Time needed for staff to teach mothers/parents/families •Knowledge of staff •Staff views

			•Costs

6. Study designs

Studies designs considered in this review will include systematic reviews (SRs), randomised controlled trials (RCTs), and other study designs - as long the study evaluates the effectiveness of an intervention. Case studies will not be included in the review.

7. Search strategy

This level of searching involves searching a range of medical, nursing, psychological and midwifery databases. All databases will be searched from inception date and searches will not be limited by study design, country or language.

The following databases will be searched:

- MEDLINE & MEDLINE In-Process Citations
- EMBASE
- PsycINFO
- Science Citation Index
- CINAHL
- British Nursing Index
- Sociological Abstracts
- Pascal
- LILACS
- ASSIA
- Midwifery and Infant Care

Unpublished research or research reported in the grey literature will be sought by searching a range of relevant databases including:

- Inside Conferences
- Index to Theses
- Dissertation Abstracts
- Cochrane Central Register of Controlled Trials
- metaRegister of Controlled Trials
- National Research Register
- HMIC

Websites of relevant stakeholder organisations will also be scanned.

7.1. Terminology

The terms for the search strategies were identified through discussion between an Information Officer and the research team, by scanning the background literature, and by browsing the MEDLINE Thesaurus (MeSH).

7.2. Handsearching

Key journals identified during inclusion screening will be hand searched as will the bibliographies of studies retrieved. Attempts to identify further studies will be made by contacting experts in the field and stakeholder organisations.

7.3. Reference management and documentation

As several databases will be searched, some degree of duplication will result. In order to manage this issue, the titles and abstracts of bibliographic records will be downloaded and imported into Endnote bibliographic management software and duplicate records removed. Full details of the search process will be recorded.

Searches for economic evaluations will also be undertaken in the databases listed above. The search strategy will be adapted to focus on economic evaluations using search terms derived from the strategies used to identify studies for inclusion in NHS EED (see http://nhscrd.york.ac.uk/nfaq2.htm). Additional searches of the following database will be undertaken:

- NHS Economic Evaluation Database (NHS EED)
- Health Economic Evaluation Database (HEED)
- Pediatric Economic Evaluation Database (PEDE)

Further searches will be undertaken to help populate the decision model, although where possible studies identified through the systematic review will be utilised.

The following search strategy will be used in MEDLINE, and subsequently translated and adapted for use in other databases:

1. Breast Feeding/
2. breastfe$.ti,ab.
3. (breast$ adj2 (fed$ or feed$)).ti,ab.
4. Lactation/ or Milk, Human/
5. (breastmilk$ or lactat$).ti,ab.
6. (transitional care and (maternal$ or mother$ or baby or babies or infant$ or newborn$ or neonat$ or neo nat$ or perinat$ or peri nat$ or premie or premies)).ti,ab.
7. ((breast$ or mother$ or human or maternal$) adj2 milk).ti,ab.
8. (nursing adj2 (maternal$ or mother$ or baby or babies or infant$ or newborn$ or neonat$ or neo nat$ or perinat$ or peri nat$ or premie or premies)).ti,ab.
9. ((maintain$ or maintenance$ or establish$ or begin$ or start$ or commenc$ continu$ or sustain$ or prolong$ or extend$) adj2 (milk or breast$ fed$ or breast feed$ or lactat$ or nursing or suck$ or breastfed$ or breastfeed$)).ti,ab.
10. ((milk or breastmilk) adj2 (donor$ or donat$ or bank$)).ti,ab.
11. ((milk or breast$) adj2 express$).ti,ab.
12. (breast pump$ or breastpump$).ti,ab.
13. (hand$ adj2 express$).ti,ab.
14. kangaroo.ti,ab.
15. ((skin$ adj2 contact) or skin-to-skin).ti,ab.
16. (suck$ adj2 breast$).ti,ab.
17. (tube adj2 (feed or fee$)).ti,ab.
18. (cup adj2 (fed or fee$)).ti,ab.
19. (bottle adj2 (fed or fee$)).ti,ab.
20. (transition adj2 breast$).ti,ab.

21. Lactation Disorders/nu, di, dh, pc, dt, th [Nursing, Diagnosis, Diet Therapy, Prevention & Control, Drug Therapy, Therapy]
22. Galactorrhea/di, dh, nu, pc, dt, th
23. (Galactagogue$ or caffeine or hops or fenugreek or fennel seed$ or blessed thistle or domperidone or alfalfa).ti,ab.
24. Caffeine/tu [Therapeutic Use]
25. Humulus/ or Plants, Medicinal/tu or Metoclopramide/tu or Sulpiride/tu or Plant Extracts/tu or Chlorpromazine/tu or Dopamine Antagonists/tu or Oxytocin/tu or Thyrotropin-Releasing Hormone/tu or Human Growth Hormone/tu
26. Trigonella/ or (Sulpride or metoclopramide or domeperidone or chlorpromazine or oxytocin or dopamine antagonist$ or thyrotropine releasing hormone$ or TRH or human growth hormone$).ti,ab.
27. Foeniculum/ or creamatocrit$.ti,ab.
28. Cnicus/
29. Domperidone/tu [Therapeutic Use]
30. Medicago sativa/
31. (nipple$ shield$ or breast$ shield$).ti,ab.
32. (dropper$ adj2 (fed or fee$)).ti,ab.
33. (spoon adj2 (fed or fee$)).ti,ab.
34. (syringe$ adj2 (fed or fee$)).ti,ab.
35. supplementer$.ti,ab.
36. Pacifiers/
37. (pacifier$ or dummy or dummies or soother$).ti,ab.
38. (non-nutritive suck$ or nonnutritive suck$).ti,ab.
39. Rooming-in Care/
40. (rooming-in or room-in or co-sleep$).ti,ab.
41. (bedshar$ or bed-shar$).ti,ab.
42. ((bedside$ or bed side$) adj2 (cot or cots or cradle$ or crib or crib)).ti,ab.
43. or/1-42
44. Intensive Care Units, Neonatal/
45. Intensive Care, Neonatal/
46. (nicu or nicus).ti,ab.
47. (scbu or scbus).ti,ab.
48. ((special or intensive or icu$) adj3 (newborn$ or neonat$ or baby or babies or infant$ or neonat$ or neo nat$ or perinat$ or peri nat$ or premie or premies)).mp.
49. ((newborn$ or neonat$ or baby or babies or infant$ or neonat$ or neo nat$ or perinat$ or peri nat$ or premie or premies) adj2 unit$).mp.
50. or/44-49
51. 43 and 50
52. Health Promotion/
53. (promotion$ or promoting).ti,ab.
54. promot$.ti,ab.
55. Inservice Training/
56. ((staff or professional$ or nurse$ or doctor$ or physician$ or midwife$ or midwive$) adj2 training).ti,ab.
57. social support/
58. ((family or families or parent$ or mother$ or father$ or partner$) adj2 support$).ti,ab.

59. (antenatal educat$ or ante natal educat$ or neonatal educat$ or neo natal educat$ or prenatal educat$ or pre natal educat$ or preconception$ educat$ or pre conception$ educat$).ti,ab.
60. (postpartum educat$ or post partum educat$ or postnatal educat$ or post natal educat$).ti,ab.
61. ((family or families or parent$ or mother$ or father$ or partner$) adj2 involv$).ti,ab.
62. (early adj2 discharge$).ti,ab.
63. ((family or families or parent$ or mother$ or father$ or partner$) adj2 attitude$).ti,ab.
64. ((staff or professional$ or nurse$ or doctor$ or physician$ or midwife$ or midwive$) adj2 attitude$).ti,ab.
65. Patient Education/
66. ((peer$ or social$ or interpersonal$ or inter personal$ or midwife$ or midwive$ or profession$ or practitioner$ or nursing or lactation) adj2 (encourag$ or motivat$ or support$ or guid$ or counsel$ or consult$ or advic$ or advis$)).ti,ab.
67. (lactation adj2 (consultant$ or expert$ or adviser$ or specialist$ or advisor$)).ti,ab.
68. (humane adj2 (prematur$ or pre matur$ or premie or premies or perinat$ or peri nat$ or neonat$ or neo nat$) adj1 care).ti,ab.
69. ((tallin or Levin) adj1 (method$ or approach$ or program$ or propos$ or unit$)).ti,ab.
70. ((mother$ or parent$ or maternal$ or famil$) adj1 (led or focus$ or lead$ or direct$ or center$ or centre$) adj2 care).ti,ab.
71. (abm or lll or bfi or bfhi or nct).ti,ab.
72. (association of breastfeeding mothers or association of breast feeding mothers).ti,ab.
73. (la leche league or national childbirth trust).ti,ab.
74. (baby friendly or breaststart or breast start or beststart or best start or nidcap).ti,ab.
75. (support$ strateg$ or support$ system$ or support$ program$).ti,ab.
76. (Neonat$ Individuali?ed Developmental Care and Assessment Program$).ti,ab.
77. (Newborn$ Individuali?ed Developmental Care and Assessment Program$).ti,ab.
78. or/52-77
79. 50 and 78
80. 51 or 79
81. animal/
82. human/
83. 81 not (81 and 82)
84. 80 not 83
85. 84 not (letter or comment or editorial).pt.

7.4. Study selection criteria and procedures

Two reviewers will independently screen titles and abstracts of potentially relevant literature using an Endnote database compiled by the Information Officer (Kate Misso). Any disagreements will be resolved by consensus. Any references/studies identified by handsearching, or by contacting experts in the field will be entered on the Endnote database – and screened using the same procedure. Full papers will be ordered and assessed for inclusion (using a checklist) by one reviewer and checked by a second. Any disagreements on whether or not a paper is relevant to the review will be resolved by a third reviewer. For this review, the three reviewers involved will be Sarah King, Felicia McCormick and Elizabeth Stenhouse.

7.5. Study quality assessment checklists and procedures

The quality of the individual studies will be assessed using modified checklists from CRD's Report No.4 (Centre for Reviews and Dissemination, 2001) (or a later version). Quality assessment will be carried out by one reviewer and checked by a second. Any disagreements will be resolved by a third reviewer.

The quality assessment of economic evaluations will be based on a modified version of the Drummond checklist, which consists of a 36-item checklist (Drummond and Jefferson, 1996). The assessment will distinguish between studies that relate costs to an intermediate measure of effectiveness (such as rates of breastfeeding initiation, duration of breastfeeding, breastfeeding rates at discharge from SCBU/NICU) and those that have sought to relate costs to a disease specific measure or preference measure (eg attitudes of mothers), and infant health measures (eg reduction in cases of necrotising enterocolitis, gastrointestinal disease).

7.6. Data extraction strategy

Data will be extracted by one reviewer and checked by a second reviewer. An example of a simple data extraction sheet is presented in Appendix A. The detail of information required will be discussed (and checked with appropriate Advisory Group members if needed) and the data extraction forms piloted before a final version is agreed.. Any disagreements in the information extracted will be checked and resolved by a third reviewer.

8. Synthesis of the extracted evidence

8.1. Combining the data

Data will be combined using meta-analysis and presented in forest plots where possible (i.e. if the data is not heterogeneous). It is likely, however, that most of data will be presented using a narrative synthesis as the physical conditions of the babies will differ within and between NICU and SCBU settings. In addition, definitions of NICU and SCBU may differ among studies, so that it may not always be meaningful to categorise the interventions by setting.

8.2. Decision Modelling

The systematic review will be used to develop and populate a decision analytical model. The Information Officer will work in close liaison with the health economist to identify the model questions. Additional information to answer these questions will be provided by focused searching of the appropriate databases and statistical sources. It is anticipated from the scoping searches that the volume of economic evaluations meeting the inclusion criteria is likely to be low, and may need to be augmented with other sources of relevant information, including epidemiological studies, outcome data gained from current SCBU/NICU settings and from expert clinical opinion. The objective of modelling will be to synthesise clinical data with resource use, costs, and relevant outcomes of interest from a variety of sources.

The purpose of the model will be to evaluate the cost-effectiveness of the methods of supporting and encouraging breastfeeding compared to current practice, capturing any health benefits of breastfeeding, for infants who spend (some) time in SCBU/NICU. The analysis will be conducted from the perspective of the NHS. It is anticipated that the time horizon for the model will be one year, and, as such, discounting of costs/benefits will not be appropriate. However, if data are available to extend the time horizon of the model then this will be considered and discounting will be conducted in line with the NICE Reference Case recommendations (NICE 2004).
The appropriate structure of the model cannot be determined in advance of the project commencement. Development of the structure will be closely linked to the findings of the systematic review and the expert opinions of the clinical collaborators, reviewers and Advisory Group members. The uncertainty in the model will be captured through sensitivity analyses (probabilistic modelling and deterministic). The results obtained will be

expressed using incremental cost-effectiveness ratios (ICERs) and/or cost-effectiveness acceptability curves (CEACs) where relevant.

We expect there to be limited data on the health implications for preterm infants, but we will use all available evidence including data from studies of term babies if appropriate, and we will make explicit all assumptions used to estimate cost per QALY. Where QALYS can be estimated from the data available, CEACs will show the probability of the treatments being cost-effective over a range of values that NHS decision makers may be willing to pay per additional QALY. Given that one of the objectives of modelling is to assess uncertainty and gaps in evidence, an expected value of perfect information analysis (EVPI) will be calculated, if feasible, to ascertain the cost of the uncertainty in the model.

8.3. Identifying future research priorities

As the objective of this review is to identify and synthesise available evidence, we will not attempt to answer research questions if intervention studies are not available. Gaps in the evidence will be identified in the course of the systematic review, and information on barriers to change may become evident.

Advisory Group input, including case study work, will be used to examine those gaps and identify other potential interventions. Research priorities will be agreed by the Advisory Group and collaborators. Each research priority identified will be annotated to demonstrate its provenance (ie the literature from which it is drawn, and/or the group that considers it to be a priority and why).

8.4. Case studies

In addition to the systematic review, we will present two to three case studies in settings where breastfeeding/breast milk feeding initiation and promotion have been successful and sustained. The organisation of care and factors identified as important by staff in these settings will be examined.

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Appendix A Template for data extraction table

First author Year Country Study design Quality	Study population	Research question	Intervention	Main results	Confounders / Comments