International Journal of Technology Assessment in Health Care, **26:2** (2010), 133–140.

doi:10.1017/S0266462310000115

ASSESSMENTS

Economic evaluation of enhanced staff contact for the promotion of breastfeeding for low birth weight infants

Stephen J. C. Rice, Dawn Craig, Felicia McCormick, Mary J. Renfrew
University of York

Anthony F. Williams
University of London

Objectives: There is evidence that breastmilk feeding reduces mortality and short and long-term morbidity among infants born too soon or too small. The aim of this study was to evaluate the cost-effectiveness of enhanced staff contact for mothers with infants in a neonatal unit with a birth weight of 500–2,500 g from the perspective of the UK National Health Service.
Methods: A decision-tree model linked clinical outcomes with long-term health outcomes. The study population was divided into three weight bands: 500–999 g, 1000–1,749 g, and 1,750–2,500 g. Clinical and resource use data were obtained from literature reviews. The measure of benefit was quality-adjusted life-years. Uncertainty was evaluated using cost-effectiveness acceptability curves and sensitivity analyses.
Results: The intervention was less costly and more effective than the comparator in the base–case analysis for each birth weight group. The results were quite robust to the sensitivity analyses performed.
Conclusions: This is the first economic evaluation in this complex field and offers a model to be developed in future research. The results provide preliminary indications that enhanced staff contact may be cost-effective. However, the limited evidence available, and the limited UK data in particular, suggest that further research is required to provide results with confidence.

Keywords: Cost-effectiveness, Infants, Low birth weight, Breastmilk, Staff contact

There is evidence that breastmilk feeding reduces mortality and short and long-term morbidity among infants born too soon or too small (14;23). In 2005, initiation rates of breastfeeding in special care baby units were greater than those in the general population. Bolling et al. (2) found that the breastfeeding rate at 1 week was 63 percent in the general population and 68 percent among infants starting life in neonatal units. Neonatal units include both neonatal intensive

The study was funded by a grant from the National Institute for Health Research Health Technology Assessment programme: grant no 06–34/02. This paper does not represent the views of the NIHR or the Department of Health. Input without contributing to the paper: Kate Misso contributed to the design of searches of the literature for evidence and references management; and Lisa Dyson, Sarah E. King, and Elizabeth Stenhouse contributed to the design of the study. Advisory Group: Gene Anderson, Rosie Dodds, Sandra Lang, Shelley Mason, Paula Meier, Josephine Patterson, Mark Sculpher, Sarah O'Sullivan, Amanda Sowden, Louise Wallace. Additional expert input: Nick Embleton, Alan Fenton, Elizabeth Jones, Caroline King, Camilla Kingdon, Paula Sisk, Gillian Weaver: and four anonymous peer reviewers.

care units and special baby care units. Nevertheless, health benefits could still be reaped by increasing these rates further and in particular by enabling infants to breastfeed exclusively. Furthermore, there is the possibility of significant cost-savings if complications resulting in long-term disability can be reduced by consumption of breastmilk (32). Promoting initiation, duration, and exclusivity of breastmilk is a public health priority nationally and internationally and is considered an important mechanism for addressing health inequalities (7;12;35), and it is particularly important in this vulnerable group.

A health technology assessment was conducted on the clinical effectiveness and cost-effectiveness of breastfeeding promotion for infants in neonatal units (25). This study reports the cost-effectiveness analysis part, which had a study population of mothers with infants in a neonatal unit with low birth weight. Here, low birth weight is defined as 500–2,500 g. The cost-effectiveness analysis uses clinical evidence summarized in the effectiveness review reported elsewhere (26). A systematic review of the literature for economic evaluations of promotional strategies for breastfeeding in neonatal units was conducted. No economic evaluations that met the inclusion criteria were identified.

A wide range of factors determine the incidence and prevalence of breastfeeding. In the case of neonatal units these additionally include feeding methods, methods of expressing breastmilk and staff training, as well as public health interventions. The effectiveness review examined several of these. The cost-effectiveness analysis focused on evaluating enhanced staff contact. This consisted of providing individualized education, support and care plans to mothers of infants in neonatal units by specially trained staff. The two intervention studies used in this analysis involved either training to International Board Certified Lactation Consultant (9) or training in the benefits of and barriers to breastfeeding, physiology of lactation, use of breast pumps, prefeeding interventions based on synactive theory, and breastfeeding interventions acknowledging readiness to infant (22).

Our study has used these data to evaluate the cost-effectiveness from a National Health Service perspective of enhanced staff contact compared with normal staff contact over the lifetime of an infant admitted to a neonatal unit with low birth weight. It was assumed that breast pumps and facilities for milk expression and storage were freely available. Normal staff contact is an absence of nurses specifically trained to support breastfeeding mothers.

METHODS

Model

The problem was modeled using a decision tree developed in Treeage Pro 2007. The data reviewed for the decision analysis were applicable to mothers with infants in neonatal units with a birth weight between 500 g and 2,500 g. This theoretical population was divided into three birth weight subpopulations: 500 g to 999 g; 1,000 g to 1,749 g; and 1,750 g to 2,500 g. These weight bands were considered appropriate because the incidence of disease increases as the birth weight decreases (8;10).

The prevalence of feeding with mothers' milk depends on whether or not the mother originally intended to breastfeed before being encouraged to express milk in the neonatal unit (28). Thus in part 1 of the decision tree, the population that receives enhanced staff contact is divided into those who intended to breastfeed (ITB) and those who did not (NITB) before childbirth (Figure 1). The effectiveness estimate for the study intervention, which concerns increasing breastfeeding rates/feeding with breastmilk, is for all mothers regardless of whether or not they intended to breastfeed.

There is a relationship between the proportion of the total milk intake that is breastmilk and a disease protective effect (34). Convenient categories of levels of breastmilk intake that can be identified in the literature: formula only (F), some mothers' milk plus formula (MM+F) or donor milk, and mostly mothers' milk (MM). Mostly mothers' milk was defined as greater than 80 percent of total milk intake. Consequently, in the tree the infants of both ITB and NITB mothers received either MM, MM+F, or F. Each of these groups of infants was considered to be at risk of one of six possible feeding-related outcomes during the neonatal stay: medical necrotizing enterocolitis (NEC), Bell stage II or greater; surgical NEC; fungal sepsis, Gram-negative sepsis, or Gram-positive sepsis; no NEC or sepsis. These were considered by clinical experts to be the most significant clinical events affected by the consumption of breastmilk. Rehospitalization rates were not included. Due to limited space, the events for every chance node in Figure 1 are not shown. The nodes with the same numbers share the same possible following events. Every chance node labeled 3 follows with death or survival as shown in part 2 of the decision tree.

An infant with any of these six clinical outcomes might survive or die. Survivors might or might not develop a long-term neurodevelopmental impairment (NDI). Those who do develop a long-term NDI were considered to have mild, moderate, or severe disability.

As these conditions were considered to be long-term, the time horizon of the analysis was lifetime. Each health state was allocated utility, life expectancy, and cost values.

A second, identical population of infants passed through the same tree with normal staff contact rather than enhanced staff contact. The corresponding outcome probabilities were different. The model calculated the expected quality-adjusted life-years (QALYs) and cost per patient for each comparator and an incremental analysis was then performed.

Clinical Data

A baseline intention to breastfeed rate of 72 percent for England and Wales was taken from the Infant Feeding Survey

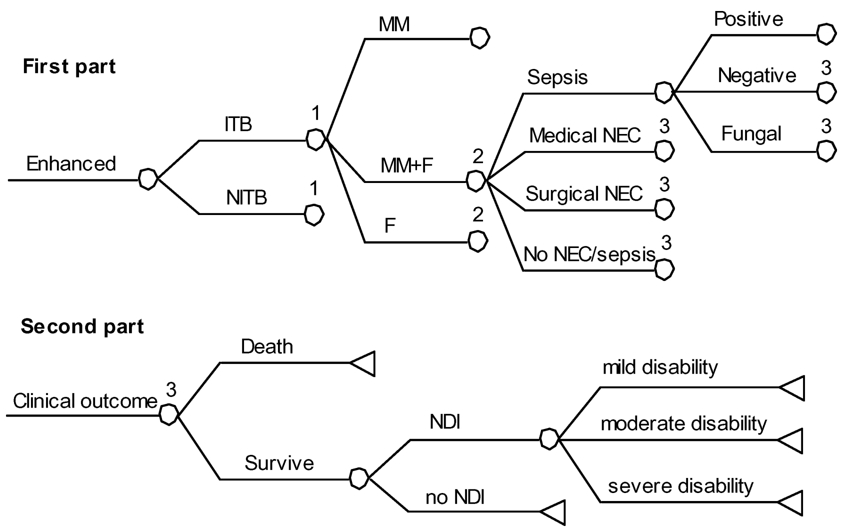

Figure 1. The decision tree for the enhanced staff contact intervention. Circles indicate that the following states are due to chance. A triangle indicates that the preceding state is the end state. The nodes with the same numbers share the same possible following events. The second part of the decision tree follows on from the first part where node 3 in the second part corresponds to node 3 in the first part.

2005 (2). The distribution of the three levels of mothers' milk consumption (MM, MM+F, and F) for mothers who intended to breastfeed and for those who did not, given enhanced staff contact, was obtained by personal communication from the author of the only paper (28) with such data that was identified in the searches for the effectiveness review (26) (see Supplementary Table 2, which is available at www.journals.cambridge.org/thc2010010).

To obtain the distribution of these different levels of mothers' milk consumption for normal staff contact, we needed the odds ratio of an infant receiving his or her own mothers' milk during neonatal stay given normal staff contact compared with enhanced staff contact. This required studies comparing the two interventions for all mothers with infants in neonatal units regardless of whether or not they intended to breastfeed before birth. A pooled odds ratio weighted by sample size was derived from two relevant papers identified from the effectiveness review (9;22) (see Table 1). One study (9) studied the introduction of a lactation consultant and the other (22) studied the introduction of staff education and leaflets, both with a view to improve the encouragement and advice on breastfeeding that mothers with infants in neonatal units receive. Both were before and after studies from the United States which considered all mothers with infants in a neonatal unit. In the base case, it was assumed that the pooled odds ratio was the same for both ITB and NITB mothers.

To identify the evidence for breastmilk effectiveness on the six clinical outcomes, MEDLINE and in-process citations, EMBASE, NHS EED, HEED, and Econlit were searched from 2003 to February 2008, and the references of the identified papers reviewed. This search provided the following data: the incidence given mothers' milk and formula supplements and odds ratios of sepsis given different milk consumption (8), medical NEC (10;18;27), surgical NEC (10;18;27); the distribution of positive, negative, and fungal sepsis (27;30;33); and the incidence and OR of mortality (8;11;13;30) and NDI given each health outcome (13;16;29) (see Supplementary Tables 1 and 2, which are available at www.journals.cambridge.org/thc2010010).

The papers selected had to include adequate information to calculate odds ratios comparing outcomes for MM, mothers' milk plus donor milk (MM+D), MM+F, and F.

Supplemental literature searches identified a paper, Larroque et al. (16), published in March 2008 that provided the incidence of NDI given no disease and the distribution of mild, moderate, and severe NDI given some degree of NDI for children of 5 years of age. These "Larroque" disability states are listed in column 2 of Supplementary Table 3, which is available at www.journals.cambridge.org/thc2010010. It was assumed that this distribution of NDI states would persist for life.

The life expectancy for infants in these long-term disability states was taken from Colbourn et al. (4), which used Office of National Statistics (ONS), published data and assumptions to determine life expectancy for infants with no, mild, and severe disability. See Table 2.

Utilities

NHS EED, HEED, Econlit, and MEDLINE were searched for utility data for health states given different clinical outcomes for the population of interest. Preference was given to EQ-5D data. One study (21) provided EQ-5D utility data

https://doi.org/10.1017/S0266462310000115 Published online by Cambridge University Press

Table 1. Odds ratios used in model

Odds of ever receiving own mothers' milk	Odds ratio	SE	Reference
Normal vs enhanced staff contact	0.500	0.20	28;34
Odds of confirmed NEC (medical and surgical)			
MM vs MM and Donor	0.885	0.69	27
MM and Donor vs MM and Formula	0.465	0.66	18
Formula vs MM and Formula	3.006	0.40	18
Odds of sepsis			
MM vs MM and Donor	0.709	0.38	27
MM and Donor vs MM and Formula	0.997	0.34	27
Formula vs MM and Formula	0.803	0.15	33
Odds of mortality			
Gram +ve sepsis vs no NEC/sepsis	1.609	0.12	30
Gram -ve sepsis vs no NEC/sepsis	7.263	0.14	30
Fungal sepsis vs no NEC/sepsis	5.969	0.18	30
Medical NEC vs no NEC/sepsis	2.055	0.14	11
Surgical NEC vs no NEC/sepsis	3.124	0.12	11
Odds of NDI			
Sepsis vs no NEC/sepsis	2.282	0.07	29
Medical NEC vs no NEC/sepsis	1.187	0.19	11
Surgical NEC vs no NEC/sepsis	1.985	0.19	11

NEC, necrotizing enterocolitis; MM, mother's milk; NDI, neurodevelopmental impairment.

Table 2. Utility, life expectancy, and cost data used in the model

	Mean	SD	Reference
Utilities			
No disability	0.940	0.12	4
Mild disability	0.850	0.10	4
Moderate disability	0.645	0.12	4
Severe disability	0.470	0.25	4
Life expectancy (years)			
No disability	78.5		4
Mild disability	78.5		4
Moderate disability	67.8		4
Severe disability	26.1		4
Minutes of staff contact time			
Initial contact	45		34
Further contact	150		34
Unit costs (£)			
Registered nurse (£/hour)	41.12		5
Level 1 neonatal unit	939.00	310.20	7
Level 2 neonatal unit	671.00	178.38	7
Special Care Baby Unit	405.00	99.80	7
Major neonatal diagnosis	1514.00	838.10	7
200 mls of Formula milk[a]	1.36		3
1 Litre of Donor milk[a]	289.12		15
Expression sets per day[a]	8.40		[b]
Annual cost of disabilities (£)			
No disability	0.00		4
Mild disability	541.07		4
Moderate disability	541.07		4
Severe disability	21,500		4

[a]Included in sensitivity analyses only.
[b]By personal communication.

for permanent sequelae given childhood bacterial meningitis. The authors presented vignettes to 28 pediatricians in the Netherlands for seven case descriptions. In line with the approach taken by Colbourn et al. (4), utilities for mild, moderate, and severe disabilities were derived from these seven case descriptions by grouping them into three clusters of severity and taking the average. The result was that utilities determined for the "Colbourn" health states listed in column 3 in Supplementary Table 3, which is available at www.journals.cambridge.org/thc2010010, were used for the corresponding "Larroque" health states listed in column 2.

Cost Data

The study perspective was the NHS. The costs included in the analysis were the intervention costs; treatment of confirmed NEC and sepsis; inpatient stay in level I, II, and III units; and the lifetime cost of disability.

The cost of formula milk, donor milk, milk expression pumps, and disposable milk expression kits are all affected by the employment of enhanced staff contact. These were included in the cost of an inpatient stay in a neonatal unit. They were not included as independent cost items in the base–case analysis because no estimate of the actual cost of the provision of breast pumps per infant was available. It was inappropriate to exclude breast pump costs and not formula milk costs as independent cost items. These costs were investigated through sensitivity analyses.

The price year was 2006. All costs were valued in pounds sterling. All costs were inflated using the health component

https://doi.org/10.1017/S0266462310000115 Published online by Cambridge University Press

of the consumer price index. All costs were discounted at a rate of 3.5 percent (20).

The cost of the intervention was the extra time dedicated to mothers by specially trained staff. The minutes of staff contact time were derived from Gonzalez et al. (9), and the hourly cost of a registered nurse was derived from the Unit Costs of Health and Social Care 2006 (5) (see Table 2).

The incremental cost incurred from an episode of sepsis or NEC involves the additional disease-specific cost of treatment, the additional cost due to increased length of stay in level I, II, and III units, and the additional cost due to lifetime disability. The cost of a sepsis or NEC illness episode was assumed to be closest to a major neonatal diagnosis quoted in the NHS Reference Costs (7). The unit cost of 1 day's stay in each unit of levels I, II, and III were also obtained from the NHS Reference Costs (7).

For data on length of stay for different clinical outcomes, the papers identified from the literature search on breastmilk effectiveness were reviewed. Two U.S. studies (8;30) provided length of stay for neonatal infants with sepsis and one study provided length of stay for neonatal infants with either medical or surgical NEC. The length of stay data reported in Supplementary Table 4, which is available at www.journals.cambridge.org/thc2010010, for a level I unit represent the incremental length of stay for sepsis and NEC outcomes compared with no NEC/sepsis, hence, the length of stay of 0 days for the control. Infants that died were given an estimate of 20 days stay in a level I unit. It was assumed that this covered the cost of treatment for an infant that died in a neonatal unit.

The cost of disability was identified from a search for papers with cost data for the health outcomes for preterm infants. Trotter et al. (32). identified costs for mild, moderate, and severe disability given survival of meningococcal disease, using the Unit Costs of Health and Social Care 2000.

For sensitivity analyses, the unit cost of 200 ml of formula milk was derived from the British National Formulary. The unit cost of 1 liter of donor milk was derived from a report to the Department of Health of the Breastmilk Banking Working Group in 2003 (3). The quantity of milk per kg of the infant consumed was assumed to increase to 150 ml/kg from 60 ml/kg and remain there for the rest of the inpatient stay. The rate of increase depended on the birth weight. The cost of a single use expression kit was £1.20 (Camilla Kingdon, personal communication). It was assumed that an average of seven such sets would be used every 24 hours.

Uncertainty

A probabilistic sensitivity analysis was conducted with a theoretical cohort of 10,000 patients to explore uncertainty in the model parameters. Binary probabilities and multiple event probabilities, odds ratios, and cost and utility estimates were given beta, Dirichlet, and gamma distributions, respectively. The results are reported using cost-effectiveness acceptability curves (CEACs).

One-way sensitivity analyses were conducted, where one parameter is varied while the rest are kept constant, to explore the effect of changes in model assumptions and different parameter estimates on the cost-effectiveness results. The effect of including costs of formula feeding, provision of donor milk supplements and expression kits was evaluated. Because of the varied availability of donor milk across the country and the relatively high cost of its provision, a policy of allocating donor milk only as a supplement to mothers' milk was evaluated in sensitivity analyses. Donor milk outcome probabilities were added to the model.

The effect on the results of the treatment effect being based solely on Gonzalez et al. (9) rather than a pooled estimate from two papers due to slightly different interventions was investigated. The effectiveness of the intervention may vary depending on whether or not the mother intended to breastfeed before childbirth, so a sensitivity analysis was conducted with an odds ratio of 0.4 for those mothers who intended to breastfeed and 0.6 for those who did not and vice versa. The intention to breastfeed proportion was varied from 50 percent to 90 percent as it varies significantly between regions in the United Kingdom (2). The odds of confirmed NEC given formula feeding alone compared with mothers' milk feeding plus formula supplements was also reduced to 1.48 from 3.01 given that one paper, which could not be used in the model, suggested a much lower effect.

Instead of a registered nurse providing the intervention at £41.12 per hour, the cost of providing a hospital midwife (£65.57 per hour) was substituted. The length of stay was halved for each of the clinical outcomes (sepsis, medical NEC, and surgical NEC) because the length of stay estimates were based on U.S. data and assumptions, and this is the major cost factor. The initial probability of a mother intending to breastfeed was varied to cover varying rates between regions and ethnic groups. The only evidence available suggested that the probability of severe disability was greater in the 1,750–2,500 g weight group than the 1,000–1,749 g weight group (16). Because this was counterintuitive, sensitivity analysis was conducted to explore the impact of a greater probability of severe disability in the 1,000–1,749 g weight group compared with the 1,750–2,500 g weight group.

RESULTS

For the base–case model, the enhanced staff contact intervention reduced overall costs compared with normal staff contact and increased the gain in QALYs for each of the birth weight groups. In other words, enhanced contact dominated normal contact (see Table 3). The lower the birth weight, the greater the cost-savings and the greater the QALY gain. This was because the incidence of NEC decreased as the birth

Table 3. Base–case results from the model

Base–case	Intervention	Cost (£)	Incremental cost	Benefits (QALY)	Incremental benefit	ICER (£/QALY)
500–999 g	Enhanced[a]	86,759		14.70		
	Normal[b]	87,345	586	14.45	−0.251	Dominated
1000–1749 g	Enhanced	56,947		21.05		
	Normal	57,240	293	21.00	−0.056	Dominated
1750–2500 g	Enhanced	47,228		21.92		
	Normal	47,294	66	21.91	−0.009	Dominated

[a]Enhanced staff contact.
[b]Normal staff contact.
QALY, quality-adjusted life-year; ICER, incremental cost-effectiveness ratio.

weight increased, which reduced the potential cost-savings and health benefits from the effectiveness of breastmilk.

For the donor milk model, the enhanced staff contact intervention was only dominant in the 500- to 999-g weight group. For the 1,750- to 2,500-g group, the cost-effectiveness ratio was £34,905/QALY. The effectiveness of the intervention resulted in more women expressing milk and, because most women provide only a portion of the milk consumed, there was increased consumption of donor milk supplementation, which increased costs. The enhanced staff contact increased health outcomes across all birth weight groups.

The probabilistic sensitivity analyses showed that, in the base–case, the enhanced staff contact intervention was highly likely to be cost-effective at any cost-effectiveness threshold (see Supplementary Figure 1, which is available at www.journals.cambridge.org/thc2010010).

The sensitivity analyses showed that, for the 500- to 999-g weight group, the only scenario in which the intervention was not dominant was where the cost of expression kits was added to the model with donor milk supplements. The cost-effectiveness ratio was £355/QALY.

For the 1,000- to1,749-g group, only the sensitivity analyses with full-cost donor milk made the intervention more costly than the comparator, but the highest cost-effectiveness ratio was only £5,550/QALY. For the 1,750- to 2,500-g group, in addition to the donor milk analyses, increasing the labor cost to that of a midwife, halving the length of stay and including the cost of single use expression kits made the intervention more costly than the comparator. The highest cost-effectiveness ratio of sensitivity analyses excluding donor milk was £5,591/QALY for the inclusion of expression kit costs.

DISCUSSION

This study links three factors: a significant reduction in NEC due to consumption of breastmilk versus formula milk; an absence of significant adverse events from the consumption of breastmilk compared with formula milk; and a relatively cheap intervention compared with the cost savings from reduced NEC. Taken together they suggest a cost-effective result, where a policy of providing donor milk as supplements only is not used.

The intervention would no longer be cost-effective if donor milk were allocated exclusively as a supplement to mothers' milk. This is because it is expensive and the intervention to increase provision of mothers' milk coincidentally increases the consumption of donor milk in this scenario.

This study focused on two outcomes (sepsis and NEC) considered to be clinically important and supported by evidence. The literature showed little effect of mothers' milk consumption on sepsis rates so the health outcomes were principally determined by the effect of mothers' milk consumption on NEC. The lack of adverse events contributes to a cost-effective result. Two possible adverse events are infection from expressing, storing, and delivering mothers' milk, and transmission of disease, for example cytomegalovirus and HIV, by means of mothers' milk. Postdischarge rehospitalization also was not included, and this may have positive or negative cost implications for the intervention. Whereas the model could be refined to include the possibility of cytomegalovirus transmission and postdischarge hospitalization, we did not consider either to be prevalent adverse health outcomes relative to sepsis or NEC in this UK population.

Given the low prevalence of maternal HIV infection (15) and low frequency of mother to child transmission (31), a high estimate of the probability of an infant in a neonatal unit contracting HIV as a result of breastfeeding would be 0.00002. Postnatal cytomegalovirus transmission by means of breastmilk is more common than HIV transmission in the United Kingdom but has not been definitively associated with long-term adverse effects (19). Pasteurization of donor milk prevents postnatal cytomegalovirus transmission but heat treatment of a mother's own milk is neither recommended nor widely practiced in the United Kingdom.

This study focused on NDI as the major long-term outcome following NEC. Some infants with NEC may develop short bowel syndrome (SBS). A proportion of the mortality, although not all, from SBS will have already been captured in the in-hospital mortality rate due to surgical NEC.

Adding the full health outcomes of SBS will increase the cost-effectiveness of breastfeeding promotion in this model. Were the model to be developed further, mortality due to NEC with and without SBS would need to be distinguished. The cost of prolonged hospital stay due to SBS survivors should be included in the model cost estimates.

This study used evidence obtained from systematic reviews of the literature to obtain the clinical effectiveness data and utilities. There were many limitations to this evidence. For example, data on the effectiveness of enhanced staff support, the incidence data for NDI, and the length of stay data in level I, II, and III neonatal units were not derived from UK studies. The health states associated with the utility estimates do not perfectly match the health states in the model. Furthermore, it was assumed that the disability states would remain constant over the lifetime of the child. No estimate of the cost of breast pumps per infant was available and a generic cost estimate of a major neonatal diagnosis was used for surgery. Ideally, the incremental cost of breast pumps, formula milk, and expression kits would be included as independent cost items in the base–case analysis. The use of non-UK data necessitated extensive sensitivity analyses.

More accurate UK data are required especially with regard to the length of stay and cost data, the effectiveness of enhanced staff contact in an average UK neonatal unit, and the long-term health outcomes of infants who experience preventable complications.

Despite these limitations, this study managed to link breastfeeding with long-term outcomes using the best available information. The model presents the minimum information required to evaluate the cost-effectiveness of enhanced staff support. As new data become available, the model can be developed in future studies.

The lack of data or existing studies in this important field is in itself a finding of interest. Without good quality data on short, medium and long-term outcomes and resource use, it is hard to make definitive cost-effectiveness conclusions about the use of a specific approach to promote breastfeeding in a neonatal setting.

Current practice in the United Kingdom and internationally varies greatly, but it is known that staff with the expertise to promote and support breastfeeding are not widely available in most countries (1;17;24). The evidence available suggests that the provision of enhanced staff contact to promote breastfeeding in neonatal units is cost-effective. However, the lack of UK-relevant evidence from high quality studies places some uncertainty around this result and suggests the need for more evidence; this model offers a basis for future studies.

SUPPLEMENTARY MATERIALS

Supplementary Table 1
Supplementary Table 2
Supplementary Table 3
Supplementary Table 4
Supplementary Figure 1
www.journals.cambridge.org/thc2010010

CONTACT INFORMATION

Stephen J. C. Rice, MSc (sjcr1@york.ac.uk), Research Fellow in Health Economics, Centre for Reviews and Dissemination, **Dawn Craig**, MSc (dc19@york.ac.uk), Research Fellow in Health Economics, Centre for Reviews and Dissemination, **Felicia McCormick**, MSc (fm510@york.ac.uk), Research Fellow, Department of Health Sciences, **Mary J. Renfrew**, RM, PhD (mjr505@york.ac.uk), Professor of Mother and Infant Health, Mother and Infant Research Unit, Department of Health Science, University of York, Heslington, York, YO10 5DD, United Kingdom
Anthony F. Williams, DPhil (Oxon), MB BS, FRCPCH (awilliam@sgul.ac.uk), Reader in Child Nutrition & Consultant in Neonatal Paediatrics, Clinical Developmental Sciences (Child Health), St. George's, University of London, Cranmer Terrance, London SW17 0RE, United Kingdom

REFERENCES

1. BLISS. *Breastfeeding or expressing for a sick or premature baby. An overview of 500 women's experiences*. London: BLISS; 2008.
2. Bolling K, Grant C, Hamlyn B, Thornton A; & BMRB Social Research. *Infant feeding survey 2005: A survey conducted on behalf of the Information Centre for Health and Social Care and the UK Health Departments*. London: The Information Centre; 2007 (accessed January 29, 2008).
3. Breastmilk Banking Working Group. *Report submitted to the Department of Health*. Unpublished. London: Department of Health; 2005.
4. Colbourn T, Asseburg C, Bojke L, et al. Prenatal screening and treatment strategies to prevent group B streptococcal and other bacterial infections in early infancy: Cost effectiveness and expected value of information analyses. *Health Technol Assess*. 2007;11:1-226.
5. Curtis L, Netten A. *Unit costs of health and social care 2006*. Kent: Personal Social Services Research Unit, University of Kent; 2006 (accessed April 8, 2008).
6. Department of Health. *Implementation plan for reducing health inequalities in infant mortality: A good practice guide*. London; Department of Health, Health Inequalities Unit; 2007.
7. Department of Health. *Reference costs 2006–2007*. London: Department of Health; 2008 (accessed April 9, 2008).
8. Fanaroff A, Korones S, Wright L, et al. Incidence, presenting features, risk factors and significance of late onset septicemia in very low birth weight infants. *Pediatr Infect Dis J*. 1998;17:593-598.
9. Gonzalez KA, Meinzen-Derr J, Burke BL, et al. Evaluation of a lactation support service in a children's hospital neonatal intensive care unit. *J Hum Lact*. 2003;19:286-292.
10. Guthrie S, Gordon P, Thomas V, et al. Necrotizing enterocolitis among neonates in the United States. *J Perinatol*. 2003;23:278-285.

11. Hintz S, Kendrick D, Stoll B, et al. Neurodevelopmental and growth outcomes of extremely low birth weight infants after necrotizing enterocolitis. *Pediatrics*. 2005;115:696-703.
12. HM Government. *PSA Agreement 12: Improve the health and wellbeing of children and young people*. London: The Stationery Office; 2007.
13. Information and Statistics Division & NHS Scotland. *Small babies in Scotland: A ten year overview 1987–1996*. Scotland: Information and Statistics Division & NHS Scotland; 1998 (accessed March 13, 2008).
14. Ip S, Chung M, Raman G, et al. Breastfeeding and maternal and infant health outcomes in developed countries. *Evid Rep Technol Assess (Full Rep)*. 2007;153:1-186.
15. Joint United Nations Programme on HIV/AIDS. *2008 report on the global AIDS epidemic*. Geneva: UNAIDS; 2008.
16. Larroque B, Ancel P, Marret S, et al. Neurodevelopmental disabilities and special care of 5-year-old children born before 33 weeks of gestation (the EPIPAGE study): A longitudinal cohort study. *Lancet*. 2008;371:813-820.
17. Liu WF, Laudert S, Perkins B, et al. The development of potentially better practices to support the neurodevelopment of infants in the NICU. *J Perinatol*. 2007;27(Suppl 2):S48-S74.
18. Lucas A, Cole T. Breast milk and neonatal necrotising enterocolitis. *Lancet*. 1990;336:1519-1523.
19. Luck S, Sharland M. Postnatal cytomegalovirus: Innocent bystander or hidden problem? *Arch Dis Child Fetal Neonatal Ed*. 2009;94:F58-F64.
20. National Institute for Health and Clinical Excellence. *Guide to the methods of technology appraisal*. London: NICE; (accessed August 5, 2008).
21. Oostenbrink R, Moll H, Essink-Bot M. The EQ-5D and the Health Utilities Index for permanent sequelae after meningitis: A head-to-head comparison. *J Clin Epidemiol*. 2002;55:791-799.
22. Pineda R. *Breastfeeding practices in the neonatal intensive care unit before and after an intervention plan*. Gainesville: University of Florida; 2006. p 99.
23. Quigley M, Cumberland P, Cowden J, Rodrigues L. How protective is breastfeeding against diarrhoeal disease in infants in 1990 England? A case-control study. *Arch Dis Child*. 2005;91:245-250.
24. Redshaw M, Hamilton K. *Networks, admissions and transfers: The perspectives of networks, neonatal units and parents*. Oxford: National Perinatal Epidemiology Unit; 2006.
25. Renfrew M, Craig D, Dyson L, et al. Breastfeeding promotion for infants in neonatal units: A systematic review and economic analysis. *Health Technol Assess*. 2009;13:1-146.
26. Renfrew M, Dyson L, McCormick F, et al. Breastfeeding promotion for infants in neonatal units: A systematic review. *Child Care Health Dev*. [Epub ahead of print].
27. Schanler R, Lau C, Hurst N, Smith E. Randomized trial of donor human milk versus preterm formula as substitutes for mothers' own milk in the feeding of extremely premature infants. *Pediatrics*. 2005;116:400-406.
28. Sisk P, Lovelady C, Dillard R, Gruber K. Lactation counseling for mothers of very low birth weight infants: Effect on maternal anxiety and infant intake of human milk. *Pediatrics*. 2006;117:e67-e75.
29. Stoll B, Hansen N, Adams-Chapman I, et al. Neurodevelopmental and growth impairment among extremely low-birth-weight infants with neonatal infection. *JAMA*. 2004;292:2357-2365.
30. Stoll B, Hansen N, Fanaroff A, et al. Late-onset sepsis in very low birth weight neonates: The experience of the NICHD Neonatal Research Network. *Pediatrics*. 2002;110:285-291.
31. Townsend C, Cortina-Borja M, Peckham C, et al. Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000–2006. *AIDS*. 2008;22:973-981.
32. Trotter C, Edmunds W. Modelling cost effectiveness of meningococcal serogroup C conjugate vaccination campaign in England and Wales. *BMJ*. 2002;324:809.
33. Vohr B, Poindexter B, Dusick A, et al. Beneficial effects of breast milk in the neonatal intensive care unit on the developmental outcome of extremely low birth weight infants at 18 months of age. *Pediatrics*. 2006;118:e115-e123.
34. Vohr B, Poindexter B, Dusick A, et al. Persistent beneficial effects of breast milk ingested in the neonatal intensive care unit on outcomes of extremely low birth weight infants at 30 months of age. *Pediatrics*. 2007;120:e953-e959.
35. World Health Organization. *Global strategy for infant and young child feeding*. Geneva: World Health Organization; 2003.