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Preventing disease and saving resources: the potential contribution of increasing breastfeeding rates in the UK

APPENDICES

Research partners

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Preventing disease and saving resources: the potential contribution of increasing breastfeeding rates in the UK. Volume 2 – Appendices

Appendix 1

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Appendix 2

Methods used for searches, economic modelling and narrative analyses

1. Searches to identify relevant evidence

1.1 Search strategies

Electronic databases which covered health care, social care and psychology were searched. The search strategies were devised to identify papers describing health outcomes related to infant feeding and then included additional terms to separate systematic reviews (Review A), UK studies (Review B), and economic evaluations (Review C). This entailed combining subject indexing terms, such as MeSH in MEDLINE, and free text search terms in the title and abstract. The search terms were identified through discussion between members of the multidisciplinary research team, by scanning background literature, and by browsing database thesauri.

Methodological search filters were used in the review of systematic reviews (Review A) and the review of economic evaluations (Review C). Searches for UK primary studies (Review B) included a set of terms to identify studies in the UK context through searches of the title, abstract, indexing, author address and other country-indicative fields. There were no language restrictions and no date limits.

Databases and search strategies are shown in Appendix 3, including details of the MEDLINE search strategies, the results of all searches, and adaptations made to the search strategies for each database searched.

1.2 Process for identifying and appraising included reviews and studies of disease and developmental cognitive outcomes, and of economic evaluations

1.21 Search results – Review A: identifying systematic reviews examining health outcomes related to infant feeding

The search results were delivered in two parts: English and non-English.

English search results

One reviewer (FM) screened the titles and abstracts (n=9,671) using a pre-screening form based on the inclusion criteria for Review A (Appendix 4). A second reviewer (AM) screened a 10% sample (n=967) as a quality check. Full papers were ordered for all citations where exclusion was not possible on the basis of citation and abstract (total of 297). A total of 214 papers were received as PDF files from journals to which the university library subscribes. Of the remaining 83, papers were ordered only when they related to what became priority outcomes (a total of four of these papers was ordered).

Non-English search results

A total of 1,419 non-English citations was identified, 638 with an English abstract. One reviewer (FM) assessed these on title and abstract, and the remainder on title only, using the same pre-screening form. A second reviewer (AM) screened a 10% sample (n=142) as a quality check. Two further papers were ordered (seven others identified had already been ordered in translation during the English search process).

1.22 Search results – Review B: Identifying UK studies examining health outcomes related to infant feeding

One reviewer (FM) screened the titles and abstracts (n=3,527) using a form based on the inclusion criteria for Review B (Appendix 4). A second reviewer (AM) screened a 10% sample (n=353) as a quality check. Full papers were ordered for all citations where exclusion was not possible on the basis of citation and abstract (total of 253).

1.23 Search results – Review C: The cost-of-illness associated with 'not-breastfeeding': a systematic examination of evidence reported from the UK and comparable industrialised countries

The search for economic evaluations of infant feeding delivered 2,415 citations in an Endnote database. One experienced reviewer who is not an economist (FM) and one economist (SP) independently piloted the screening process on the first 242 citations (10% of 2,415), using the pre-screen form shown in Appendix 4. There was full agreement between the two reviewers on the included and excluded papers. The remaining titles and abstracts (2,215/2,415) were therefore screened by one reviewer (FM). Copies of 37 papers were requested as a result of this process.

Eleven papers were reviewed and data extracted.

The results of this review, including descriptions and appraisals of the included studies, conclusions and data extraction forms, are shown in full in Appendix 5.

1.3 Identifying relevant papers from search results of Review A and Review B and identifying priority outcomes for further appraisal

The goal of this stage was to use these systematic reviews and UK studies to identify a short list of priority outcomes that had sufficient good quality, relevant evidence to inform the economic analysis. We hoped to identify short, medium and long-term disease outcomes for the child including babies in neonatal units, maternal outcomes, and developmental outcomes for the child.

Identifying the priority outcomes took place in several stages over which papers were gradually excluded as follows (see Table 2.1, below for details of numbers).

The 552 papers identified in the screening process (299 from Review A and 253 from Review B) were scanned to identify the outcomes examined, and divided into individual databases

for each outcome identified. Papers where multiple outcomes were examined, and where those outcomes were identified as priorities, were added to more than one database. Where systematic reviews included studies from both developed and developing countries, and examined priority outcomes, they were examined to identify any relevant UK studies. The numbers of possible papers identified in the screening process and allocated to different categories are shown below in Table 2.1.

Table 2.1: Numbers of possible papers (n=552) identified in the screening process and allocated to different categories

Category to which papers allocated	Number of papers allocated	Comment
Excluded	199	Not relevant – e.g. not a systematic review or UK study, not related to the topic
45 outcomes where evidence did not meet our criteria	173	Shown in Appendix 6
Papers to be further examined (categorised below)	180	These papers were included on a list for detailed examination and discussion and finally allocated to one of the categories below
Total papers from screening	**552**	
• Studies with multiple outcomes	18	One or more outcome from these studies appears in one or more of: final short list, final long list, 44 outcomes where evidence did not meet our criteria
• Final short list of eight outcomes for economic analysis	100	These were further scrutinised – details in section 4.1.1 of the main report
• Final long list of eight outcomes	62	Did not meet criteria for economic analysis. Details in section 4.1.2 of the main report
Total papers to be further examined	**180**	

Outcomes where evidence was clearly inadequate for our purposes (for example, no systematic review or UK study existed) were excluded at this stage (n=199).

Outcomes where the evidence clearly did not meet our criteria were included on a list for future research (45 outcomes, 173 papers, Appendix 6).

Outcomes where systematic reviews or UK studies that were assessed at this preliminary stage as having the potential to be adequate were included on a list of possible outcomes for inclusion (n=180).

Using an iterative process to examine the strength and relevance of evidence related to each outcome, the list was then assessed by the research team and the Advisory Group using the following criteria:

- one or more reviews or studies had been identified that a) had the potential to predict the effect size with confidence, or b) where the evidence was not conclusive but the effect size was likely to be considerable
- it was scientifically plausible that the outcome could be related to infant feeding
- the outcome was assessed as important in a UK setting
- it was possible to conduct an economic analysis.

This process included the identification of the studies with the best quality of data for our purposes. For this, we had to develop a process for agreeing the best source of data to inform our economic analyses.

1.3.1 Hierarchy of evidence and quality assessment

Randomised controlled studies in this field are very rare. We therefore anticipated that conducting analyses of available data would be complicated by methodological problems in the original studies, the limited occurrence of exclusive breastfeeding, a wide range of different measures used for feeding history and for outcomes, and different findings related to diverse settings and population groups. These factors would be likely to contribute to conflicting findings between reviews and between UK studies and reviews. We were also aware that the evidence available was likely to differ in quantity, quality and relevance between outcomes. The strategy we adopted to guide our analysis was to construct a stepped approach to identifying the best quality and most appropriate evidence, using a hierarchy of evidence appropriate for this study and which could be tailored to each outcome.

For each priority outcome, we planned to identify a primary source or sources of evidence; if possible, we planned to conduct meta-analyses to combine data from different studies. We also planned to identify alternative or corroborative evidence from other sources that could confirm the size of effect identified in the primary source. The primary source of evidence might be either a UK study or a systematic review, depending on the quality of available evidence for each outcome. The process for identifying appropriate evidence is outlined in Table 2.2 below. In addition to this hierarchy, a pre-requisite for any study used was that it reported data by infant feeding method, and that it reported adequate measures of exposure to breastfeeding and use of breastmilk substitutes.

Table 2.2: Hierarchy of evidence used for each outcome to identify the reviews and studies to inform the economic models

Level of evidence	Primary source of evidence	Corroborative evidence
Level 1	One or more UK studies: the research team had to agree that it was contemporary, large enough, good quality, adequately controlled.	Systematic reviews, UK studies not meeting Level 1 criteria. Studies from other countries identified from systematic reviews.
Level 2	Good quality meta-analysis or systematic review using studies from developed countries.	Other systematic reviews, UK studies not meeting Level 1 criteria. Studies from other countries identified from systematic reviews.
Level 3	One or more UK studies not meeting Level 1 criteria.	Systematic reviews. Studies from other countries identified from systematic reviews.
Level 4	Systematic review not meeting Level 2 criteria.	Other systematic reviews. Studies from other countries identified from systematic reviews.

As the assessment of the characteristics of appropriate studies and reviews varied between outcomes, individual discussions involving the whole research team took place to agree each primary data source. For example, the assessment of a 'large enough' study required examination of the sample size to assess that individual outcome, and that would vary according to whether the outcome was common (e.g. gastrointestinal disease) or relatively rare (e.g. necrotising enterocolitis). Assessment of 'adequately controlled' required examination of related factors (e.g. for obesity, was maternal BMI controlled?). The outcome of these discussions, and reasons for inclusion/exclusion of each study or review, are shown in the Results sections for each outcome.

1.3.2 The short list and the long list of outcomes

A short list of eight priority disease and developmental outcomes that met our criteria and where primary sources of data could be identified was agreed. These outcomes became the focus of data extraction and appraisal of quality and relevance. The shortlisted outcomes were:

- For the infant/child:
    - Gastrointestinal infection
    - Lower respiratory tract infection
    - Acute otitis media
    - Necrotising enterocolitis for babies in neonatal units
    - Sudden Infant Death Syndrome
    - Cognitive outcomes
    - Childhood obesity
- For the mother
    - Breast cancer

Outcomes included on the final long list were those where it was deemed plausible that the outcome is related to infant feeding, and evidence exists to demonstrate the relationship, but where the strength of the evidence, or the way in which outcomes or infant feeding had been measured, was inadequate to inform an economic analysis.

For example, although there is good evidence that biomarkers of cardiovascular disease such as blood pressure are adversely affected by not breastfeeding, it is difficult to extrapolate from markers of cardiovascular disease in childhood to the actual costs of cardiovascular disease in adulthood. Although this is likely to be a very expensive disease related to not breastfeeding, this outcome could therefore not be included on the final short list for economic analysis. Asthma is another example: asthma is a disease where genetics interacts with environmental factors and dietary intake, but the majority of studies in the field have not addressed this interaction, and many have not adequately considered the importance of exclusive breastfeeding. Current evidence is conflicting and this outcome, while likely to be a very expensive disease, was not included on the short list. We have included this long list to demonstrate the potential extent of the economic consequences of not breastfeeding in the UK, and to act as a research agenda for future studies of the costs of disease and developmental outcomes.

Absence of a condition from the short or long list of priority outcomes does not necessarily mean that there is no association between that condition and infant feeding; it simply indicates lack of existing good quality evidence.

Section 4.1 of the main report shows the final short list and long list following the quality assessment stage, together with their relevant citations.

1.3.3 Data extraction and quality appraisal 2

Systematic reviews and UK studies relating to the agreed shortlist were identified. Data were extracted by one reviewer (FM) and checked by another (MQ), and any difficulties discussed with MJR and on many occasions with the whole research team.

Problems encountered included:

- the poor quality of exposure measurement (initiation, duration, exclusivity) of infant feeding
- the lack of consistency in the timing of exposure measures (examples included any breastfeeding to 6-8 weeks, still breastfeeding at time of occurrence of outcome, received any breastmilk)
- the limited occurrence of exclusive breastfeeding in developed country settings, resulting in most comparisons being confounded by mixed feeding
- very few randomised controlled trials exist due to ethical and practical problems of randomising feeding methods
- the close association of feeding with socio-cultural or other relevant factors, which may or may not have been controlled for in studies or reviews
- inadequate sample sizes.

1.3.4 Final identification of priority outcomes to be modelled

Only five of the eight priority outcomes identified could be modelled quantitatively within the scope of this project. Three of the outcomes (cognitive outcomes, childhood obesity, and Sudden Infant Death Syndrome) were not amenable to a quantitative approach; their impact reaches well beyond the health service and includes other sectors and considerations. A narrative on economic issues related to these three outcomes has been conducted instead (Section 4.5 of the main report), and they serve as examples of the cross-sector impact of infant feeding.

1.4 Calculating effect measures

For each of the primary sources of data identified for each of the shortlisted outcomes, we obtained risk ratios or odds ratios as appropriate. These were obtained as follows below.

1.4.1 Definition of outcome

For each of the shortlisted disease outcomes, we identified appropriate definitions based on:

- hospitalisation
    - for gastrointestinal infection, lower respiratory tract infection, necrotising enterocolitis;
- and/or GP cases or other medically confirmed diagnoses
    - for gastrointestinal infection, lower respiratory tract infection, acute otitis media, and breast cancer.

1.4.2 Definition of exposure

For each of the shortlisted outcomes, breastfeeding was grouped as appropriate. For example, for gastrointestinal infection and lower respiratory tract infection, the evidence suggests that the protective effect of breastfeeding wears off soon after breastfeeding stops (Quigley et al, 2006; Quigley et al, 2007a). Therefore, our aim was to use a risk ratio or odds ratio which took the time-dependent nature of the exposure and outcome into account, if

this was available. For example, if an infant was breastfed until aged 3 months and got a respiratory tract infection when aged 5 months, then an odds ratio for breastfeeding for 3+ months would classify this infant as having been breastfed and having got respiratory tract infection. A more accurate odds ratio would estimate the association between 'current breastfeeding' and 'current risk of disease', and this was the preferred effect measure when available. The same conditions applied to acute otitis media and to necrotising enterocolitis.

For outcomes where breastfeeding has a longer term effect on the child (e.g. cognitive outcomes, child obesity), breastfeeding duration categories were used. Where risk ratios or odds ratios were available, we used categories which corresponded with the policy scenarios we proposed (Sections 2.1 and 2.2 below), e.g. exclusive breastfeeding for at least 4 months, exclusive breastfeeding for at least 6 months, and any breastfeeding for at least 4 months.

For breast cancer, it was appropriate to use a measure based on the total number of months a mother breastfed all her children for; i.e. the 'total duration of breastfeeding'. For example, a woman who had two children and breastfed the first one for six months and the second one for two months would have a total duration of breastfeeding equal to eight months. Again we used odds ratios which corresponded to the policy scenarios (Sections 1.4.4, 1.4.5 and 2.2 below).

1.4.3 Adjustment for confounders

For each of the shortlisted outcomes, it was appropriate to use risk ratios or odds ratios which were adjusted for confounders, since none of the included UK studies or meta-analyses were randomised controlled trials, and infant feeding is known to vary according to many socio-cultural factors. For each study, we assessed whether adjustment for confounders was deemed as adequate. For almost all outcomes, it was deemed as adequate and the factors which have been adjusted for are clearly described in the Results chapter and described in detail in data extraction tables in Appendix 11.

1.4.4 Risk ratios versus odds ratios

The formula to be used in the cost of illness models to estimate the expected number of children or women with the outcome of interest in each feeding group came from Bartick and Reinhold (Bartick and Reinhold, 2010). The differential incidence was obtained as follows: x=s/(br+1-b), where x=disease incidence in the non-breastfeeding group, s=the overall incidence of the disease in question, b=the current breastfeeding rate, r-the risk ratio in favour of breastfeeding, and xr=the incidence of the condition in the breastfeeding group. Note that this formula requires a risk ratio. For all of the shortlisted outcomes, we only had data on adjusted odds ratios rather than risk ratios. Where the risk of the outcome was rare (e.g. <10%), which was the case for most of the shortlisted outcomes, the odds ratio was used as an approximation of the risk ratio (Zhang and Yu, 1998). For the more common outcomes, we converted odds ratios to risk ratios using the method proposed by (Zhang and Yu, 1998). The changes were marginal and the new risk ratio values fell in the

95% confidence interval of the original odds ratios. This gave us enough confidence to use the original adjusted odds ratio in the economic models.

1.4.5 Population attributable fractions

We originally planned to estimate the population attributable (PAF) to estimate the proportion of cases that were attributable to 'not breastfeeding'. However, this proved to be difficult because the standard formulae for PAF (Bruzzi et al, 1985) are for exposures which result in an increased risk of disease (e.g. smoking) rather than a protective effect. Methodological details are in Appendix 8.

2. Methods of economic modelling

The aim of the economic modelling was to estimate the savings in the NHS treatment costs that could be achieved if breastfeeding rates were to increase and incremental quality adjusted life years (QALYs) that might be accrued in the case of breast cancer. Objectives were therefore to:

a) estimate current costs to the NHS of treating diseases shown to be associated with breastfeeding given current breastfeeding rates;

b) predict the impact of increased breastfeeding on selected diseases given varying rates/definitions of breastfeeding;

c) estimate potential cost-savings per year, if any, that could be achieved by moving from the current breastfeeding rates to a particular breastfeeding rate/definition;

d) estimate QALYs gained and incremental benefit[1] for reduction in breast cancer cases in a cohort of primiparous women.

For each of the disease outcomes to be modelled, one or more odds ratios[2] were selected to model the benefit of breastfeeding. The processes of selection of disease outcomes and odds ratios are described above.

The five priority outcomes to be modelled were:

1. gastrointestinal infection in infants
2. lower respiratory tract infection in infants
3. acute otitis media in infants

[1] Incremental benefit (IB) is an economic metric that combines the value of QALYs with the treatment cost to arrive at a single measure.

[2] A systematic search of literature identified odds ratios in favour of breastfeeding for varying definitions of breastfeeding. The economic modelling work described here assumes that these odds ratios approximate risk ratios and tests the uncertainty in predicted cost-saving estimates through sensitivity analyses using the 95% confidence intervals of the selected odds ratio (see Appendix 13).

4. necrotising enterocolitis (NEC) in infants in neonatal units

5. maternal breast cancer.

Variation in key elements of the studies that generated odds ratios, such as variation in the definition of breastfeeding (both in terms of exclusivity and duration) and the time period in which such benefits accrued, meant that each outcome had to be modelled separately. For acute conditions (gastroenteritis, respiratory illness and otitis media), the first year of life was considered as the time horizon for costing, whereas for maternal breast cancer it was the lifetime of a cohort of primiparous women. For NEC, it was the length of stay in neonatal units.

The perspective of the economic analysis is that of the National Health Service (NHS) in the United Kingdom. Costs associated with not breastfeeding that fall on individuals or households and/or any other sectors are excluded, as are any costs of interventions to promote breastfeeding. Data on treatment costs and potential cost savings are presented in 2009/10 prices. Where the costing time horizon is longer than a year (e.g. maternal breast cancer), a rate of 3.5% was used to discount the future stream of treatment costs in baseline estimates (National Institute for Health and Clinical Excellence, 2006).

A separate evidence review was carried out to establish the following model parameters: breastfeeding rates (current practice); incidence of outcomes; incidence of care episodes (primary and secondary) specific to the selected conditions; unit costs of treatment of the condition or unit-costs of care episodes. This review relied on most recent publications (e.g. NICE guidance, National Institute of Health Research Health Technology Assessment reports, and peer-reviewed journal articles) and hand-searching of the bibliographies of those papers. All model parameters are specific to the United Kingdom. A commentary on evidence appraisal and synthesis is included for each model and provided as Appendix 9.

2.1 The 7-step framework

A framework was developed to inform the modelling of all the outcomes identified, building on common methods adopted by previous studies (Weimer, 2001; Drane, 1997; Bartick and Reinhold, 2010). The common steps that were followed across all outcomes are set out below and in Figure 2.1.

1) Develop breastfeeding policy scenarios

The aim of the modelling exercise was to estimate the extent to which NHS treatment costs would be reduced if breastfeeding rates were increased. Therefore, various breastfeeding policy scenarios relative to a 'base case' were needed from which to simulate any cost-savings associated with increased breastfeeding. The variations in the definition of breastfeeding (both in terms of exclusivity and duration), the source of data on breastfeeding rates, and the time period in which benefits accrued due to breastfeeding meant that a 'universal' policy scenario was not applicable across the five outcomes considered. Therefore, outcome-specific policy scenarios were developed. Both the description and the rationale for these are described in the outcome-specific methods sections.

2) Determine the reference population

The reference population selected was either children born in the year 2009 (for child outcomes), sourced from data provided by the Office for National Statistics, or a cohort of primiparous women (for maternal outcome), sourced from Euro Peristat (EURO-PERISTAT project in collaboration with SCPE EUROCAT & EURONEOSTAT, 2008).

3) Divide the reference population between breastfeeding groups

The reference population was divided into two groups: breastfed children or breastfeeding women; and non-breastfed children or not-breastfeeding women, using breastfeeding rates derived from the Infant Feeding Survey (Information Centre for Health and Social Care, 2011), Bolling (Bolling et al, 2007), or from Liu et al (Liu et al, 2009) for breast cancer. This was used to estimate the expected number of children (women) who would be breastfed (breastfeeding) under each policy scenario.

4) Estimate expected number of disease/care episodes in each feeding group

The expected number of children (or women) experiencing the outcome of interest was estimated in each feeding group for each policy scenario. The differential incidence was obtained using the formula provided by Bartick and Reinhold (Bartick and Reinhold, 2010): $x= s/(br+1-b)$, where x = disease incidence in non-breastfeeding group, s = overall incidence of the disease in question, b = current breastfeeding rate, r = odds ratio in favour of breastfeeding and xr = incidence of the condition in breastfeeding group. This formula is applicable when the odds ratio approximates the risk ratio (see footnote 1 on the previous page).

5) Estimate total costs of treatment per year in each breastfeeding group under each policy scenario

The estimated number of children or women with the outcome of interest fed into the calculation of costs by estimating incidence of care episodes and multiplying by unit cost of a care episode (hospitalisation or GP visit). The costs in each feeding group were summed for total costs of the disease under each policy scenario. For maternal breast cancer, a cohort of 100,000 women were followed up over their lifetime, using a simple 3-state Markov process (cancer, no-cancer, death), to estimate the treatment costs.

6) Estimate total potential cost-savings per annum under different policy scenarios

Total treatment costs per year under each policy scenario were compared with the base case to ascertain the extent to which increasing breastfeeding rates would reduce health service costs. In the case of breast cancer, an additional metric, the incremental benefit, which combines the value of QALYs with treatment costs, was estimated. The findings present the potential savings to the NHS that might result from increased rates of breastfeeding. No attempt has been made to estimate the net benefit to the NHS, which would require subtracting the costs of the interventions used to promote and support breastfeeding. These are considered in Section 5.2 of the main report to help to contextualise the potential savings.

7) Reflecting some degree of uncertainty in predicted cost-savings

Parameters used in the modelling exercise (e.g. odds ratio and treatment costs) are derived from studies and reviews with varying characteristics (e.g. design, sample size, definition of

breastfeeding, etc). Inevitably, there is some degree of uncertainty about the point estimates reported in individual studies and in some instances the degree to which these are applicable to a UK NHS setting. Deterministic sensitivity analyses thus assessed the impact on the predicted cost-savings of the uncertainties around odds ratio and unit costs of treating the health-outcomes. These parameters were selected to capture the changes in both outcomes (expected number of cases) and costs to treat those cases. The base case estimate was altered, one at a time, in the following order:

a) Change mean value of the odds ratio for risk of hospitalisation for health-outcome in question to its lowest 95% confidence interval value
b) Change mean value of the odds ratio for risk of hospitalisation for the health-outcome in question to its highest 95% confidence interval value
c) Change national average unit cost of hospital admission for the health-outcome in question to lower quartile
d) Change national average unit cost of hospital admission for the health-outcome in question to upper quartile
e) Change unit cost of GP visit based on 11.7 minutes to unit cost of GP visit based on 17.2 minutes
f) Equalise value of odds ratio for risk of hospitalisation for 'exclusive breastfeeding' and 'any breast feeding'[3]
g) Equalise value of odds ratio for risk of GP consultation for 'exclusive breastfeeding' and 'any breast feeding'.[2]

The 7-step framework used is similar to the methods adopted by similar studies conducted in non-UK settings (Weimer, 2001, Drane, 1997, Bartick and Reinhold, 2010). However, it builds on the previous methods by:

a) including more realistic policy scenarios for four of the five outcomes (excluding NEC), based on critical analysis[4] of existing UK-specific breastfeeding data (rather than just relying on a hypothetical target);
b) limiting, to the extent possible, the use of model parameters from the same setting (UK);
c) reflecting some degree of uncertainty in final estimates of cost savings through a range of deterministic sensitivity analyses.

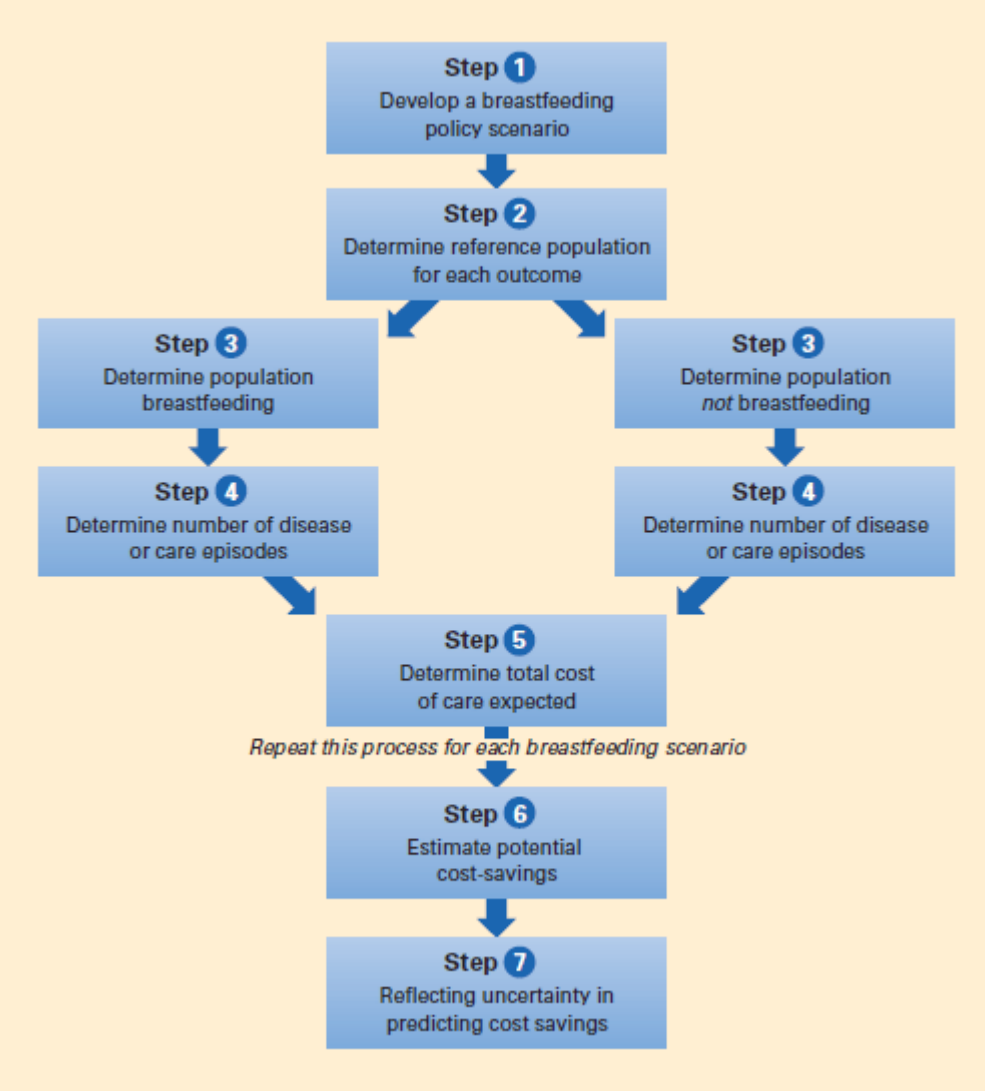
[3] The 95% confidence intervals of the odds ratios for 'exclusive breastfeeding' and 'any breastfeeding' overlapped, indicating that no significant difference exists in the risk of hospitalization or GP visits between these two definitions of breastfeeding.
[4] That is, scenarios modelled are based on the most suitable source of data and breastfeeding definitions.

In addition, the selection of risk ratios on which the current models work is the outcome of a series of structured reviews undertaken specifically for this project. Together, they make the current study more robust and relevant to the UK context.

2.2 Outcome-specific methods

The details of outcome-specific methods are given below, with a summary of the process shown in Figure 2.1.

Figure 2.1: Schematic diagram of process of economic modelling



2.2.1 Gastrointestinal infection in infants

The expected difference in costs of caring for infants below the age of one year for gastroenteritis following increases in breastfeeding are presented as potential cost-savings. The variety of alternative policy aims modelled and compared against varying definitions and rates achieved in 2005 are set out in Table 2.3. The breastfeeding rates used in Table 2.3 are from the Infant Feeding Survey 2005 (Bolling et al, 2007), as this is the most recent source of breastfeeding rates among current children and covers all four countries in the UK.

Table 2.3: Policy scenarios modelled for predicting the impact of increased breast feeding on gastrointestinal infection in infants against varying rates/definitions of breastfeeding

Definition of breastfeeding and rate used (2005) in base case	**Alternative policy scenarios modelled**		
A0: Exclusive breastfeeding (EBF) rate at 4 months (7%)	A1: increase rate of exclusive breastfeeding at 4 months to rate at 6 weeks (21%)	A2: increase rate of exclusive breastfeeding at 4 months to rate at 1 week (45%)	A3: increase rate of exclusive breastfeeding at 4 months to rate at birth (65%)
B0: Exclusive breastfeeding (EBF) rate at 6 months (0.5%)	B1: increase rate of exclusive breastfeeding at 6 month to rate at 4-months (7%)		
C0: 'any breastfeeding' rate at 6-months (25%)	C1: increase rate of 'any breastfeeding' at 6-months to rate at 6-weeks (48%)		

Data on the reference population were sourced from the Office for National Statistics (Office for National Statistics, 2010a). A total of 790,938 children were born in the UK in 2009. Applying all-cause neonatal mortality indicated 788,486 infants would still be alive in the first month of birth. This was the reference population. The largest proportion of deaths occurs in the first month and is caused by preterm birth/congenital anomalies (Office for National Statistics, 2010a). Because the post-neonatal infant mortality rate in the UK is low (about 1.4/1000), any error arising is likely to be low, as >67% of all deaths are captured by the neonatal mortality rate (Office for National Statistics, 2010b).

As breastfeeding rates increase, fewer cases of gastroenteritis in babies would be expected. Two types of health resource use following gastroenteritis were considered: GP consultations and hospital admissions.

Odds ratios from Quigley et al (Quigley et al, 2006)[5] were used to estimate impact on gastroenteritis-related GP consultations from breastfeeding. When the policy scenario involved exclusive breastfeeding (i.e. Policy A0-A3 and B0-B1), the odds ratio of 0.28 (CI: 0.11-0.69) was applied. When the policy scenario involved any breastfeeding (i.e. Policy C0-C1), the odds ratio of 0.36 (CI: 0.18-0.74) was applied.

Odds ratios from Quigley et al (2007)[5] were used to estimate impact on gastroenteritis-related hospital admissions from breastfeeding. When the policy scenario involved exclusive breastfeeding (i.e. Policy A0-A3 and B0-B1), the odds ratio of 0.39 (CI: 0.18-0.85) was applied. When the policy scenario involved any breastfeeding (i.e. Policy C0-C1), the odds ratio of 0.52 (CI: 0.30-0.87) was applied. The odds ratios used are adjusted for month (i.e. baby's age), mother's age at delivery, mode of delivery, and mother's education. This means that any estimated cost-savings would be the net of any variation in those covariates (context-specific adjustments).

Incidence of gastroenteritis-related hospital admissions in infants (17.2 per 1,000 live births) were obtained from Hospital Episode Statistics as reported in the Infant Feeding Profile (Department of Health, 2011b). The incidence of GP consultations for gastroenteritis was obtained from the Royal College of General Practice (RCGP) database and was 4,682 per 100,000 children aged <1 year[6] for the clinical diagnoses of diarrhoea, intestinal infectious diseases and non-infective enteritis and colitis.

Activity-weighted average hospital admission costs were obtained following the methods reported in the Reference Cost Guide (Department of Health 2011). First, relevant HRG procedures[7] were identified based on a mapping from the same ICD-10 codes used in hospital incidence data contained in the Infant Feeding Profile (Department of Health, 2011a)[8]. Activity-weighted unit costs were identified for the corresponding HRG procedures, multiplied by the corresponding number of activities in each procedure and summed across all included HRGs to obtain total cost. This was divided by the sum of all activities, except excess bed-day activities[9] to obtain unit cost of hospital admission due to gastroenteritis. The results are given in Appendix 9.

Unit cost of a GP visit obtained from Curtis (Curtis, 2010) was £36 (lasting 11.7 minutes). The upper value of the unit cost of a GP visit was £53, assuming a longer consultation (lasting 17.2 minutes).

[5] Re-analysis by Quigley (Quigley MA, Hockley C, Carson C, Kelly Y, Renfrew MJ, Sacker A. Breastfeeding is Associated with Improved Child Cognitive Development: A Population-Based Cohort Study. The Journal of Pediatrics. 2012;160(1):25-32).

[6] RCGP 2012 (Personal communication)

[7] Obtained from NHS Reference costs 2009-10 - Schedule 4 NHS Trust and PCT combined for non-elective short-stay, non-elective long-stay, and non-elective excess bed days.

[8] ICD-10 codes included: A09X, K521-522, K528-529. HRG4 codes mapped: PA21A-B, PA18, PB01z, PB02Z.

[9] By default, they are included in the weighted unit costs reported in the NHS Reference costs

Results are presented as annual total costs of caring for infants below the age of 1 year for gastroenteritis following increases in breastfeeding. This difference is presented as potential cost-savings from the baseline estimate.

2.2.2 Lower respiratory tract infection in infants

The policy scenarios to model the economic impact of breastfeeding on lower respiratory tract infections (LRTI) in infants were the same as gastroenteritis reported in Table 2.3. The same number of children (788,486) who formed the basis for the reference population in the gastroenteritis case study also formed the reference population for LRTI.
As breastfeeding rates increase, fewer cases of LRTI in babies would be expected among those who are breastfed compared to those who are not. Two types of health resource use following LRTI were considered: GP consultations and hospital admissions.

Odds ratios from Fisk et al (Fisk et al, 2011) and Howie et al (Howie et al, 1990) were used to estimate impact on LRTI-related GP consultations from breastfeeding. When the policy scenario involved exclusive breastfeeding (i.e. Policy A0-A3 and B0-B1), the odds ratio of 0.69 (CI: 0.47-1.0)[10] was applied (Howie et al, 1990). When the policy scenario involved any breastfeeding (i.e. Policy C0-C1), the odds ratio of 0.65 (CI: 0.43-0.96) was applied (Fisk et al, 2011).

Odds ratios from Quigley et al (Quigley et al, 2007a)[10] were used to estimate impact on LRTI-related hospital admissions from breastfeeding. When the policy scenario involved exclusive breastfeeding (i.e. Policy A0-A3 and B0-B1), the odds ratio of 0.70 (CI: 0.49-0.98) was applied. When the policy scenario involved any breastfeeding (i.e. Policy C0-C1), the odds ratio of 0.67 (CI: 0.52-0.88) was applied. The odds ratios used are adjusted for month (i.e. baby's age), mother's age at delivery, mode of delivery, and mother's education. This means that any estimated cost-savings would be the net of any variation in those covariates (context-specific adjustments).

Incidence of LRTI-related hospital admissions in infants (59.1 per 1000 live births) was obtained from Hospital Episode Statistics as reported in the Infant Feeding Profile (Department of Health, 2011a). The incidence of GP consultations for LRTI was obtained from the Royal College of General Practice (RCGP) Annual Report and was 23,433 per 100,000 children aged <1 year (RCGP 2010) for the clinical diagnosis of LRTI.

Activity-weighted average hospital admission costs were obtained following the methods reported in the Reference Cost Guide (Department of Health, 2011b). First, relevant HRG procedures[11] were identified based on a mapping from the same ICD-10 codes used in hospital incidence data contained in the Infant Feeding Profile (Department of Health,

[10] Estimated by Quigley (2012) based on Howie et al. (1990).
[11] These procedures were obtained from NHS Reference costs 2009-10 - Schedule 4 NHS Trust and PCT combined for non-elective short-stay, non-elective long-stay, and non-elective excess bed days.

2011a)[12]. Activity-weighted unit costs were identified for the corresponding HRG procedures, multiplied by corresponding number of activities in each procedure and summed across all included HRGs to obtain total cost. This was divided by the sum of all activities, except excess bed-day activities[13] to obtain unit cost of hospital admission due to LRTI. The results are given in Appendix 10 with the upper and lower quartile values used in the sensitivity analysis.

Unit cost of a GP visit was obtained from Curtis (Curtis, 2010) was £36 (lasting 11.7 minutes). The upper value of the unit cost of a GP visit was £53, assuming a longer consultation (lasting 17.2 minutes).

2.2.3 Acute otitis media in infants

The policy scenarios to model the economic impact of breastfeeding on acute otitis media (AOM) in infants were the same as gastroenteritis reported in Section 2.2.1. The same number of children (788,486) who formed the basis for the reference population in the gastroenteritis case study formed the reference population in AOM.

As breastfeeding rates increase, fewer cases of AOM in babies would be expected. As it is uncommon to admit infants to hospitals following a clinical diagnosis of otitis media and no evidence was found to show a difference in hospital admission for AOM between babies who are and are not breastfed, only one type of health resource – GP consultations – was considered.

Odds ratios from Ip et al (Ip et al, 2007) and Fisk et al (Fisk et al, 2011) were used to estimate impact of breastfeeding on AOM-related GP consultations. When the policy scenario involved exclusive breastfeeding (i.e. Policy A0-A3 and B0-B1), the odds ratio of 0.50 (CI: 0.37-0.70)[14] was applied (Ip et al, 2007). When the policy scenario involved any breastfeeding (i.e. Policy C0-C1), the odds ratio of 0.4 (CI: 0.21-0.76) was applied (Fisk et al, 2011).

Incidence of GP consultations for otitis media was obtained from the Royal College of General Practice (RCGP) Annual Report and was 136 per 100,000 children aged <1 year (RCGP 2010) for the clinical diagnosis of AOM.

Unit cost of a GP visit was obtained from Curtis (Curtis, 2010) and was £36 (lasting 11.7 minutes). The upper value of the unit cost of a GP visit was £53, assuming a longer consultation (lasting 17.2 minutes).

[12] ICD-10 codes included: J050; J101; J111; J100; J110; J121; J129, J13X; J14X; J152; J153: J154; J159; J168; J180; J181; J88; J189; J206; J208; J209; J22X; J108; J118; J120; J122; J128; J150; J151; J156-J158; J170-J173; J210;J218;J219; HRG4 codes mapped: PA65A; PA65B; PA65C; PA14C; PA14D; PA14E; WA06W; WA06Y; DZ11C; PA15A; PA15B.
[13] By default, they are included in the weighted unit costs reported in the NHS Reference costs
[14] Estimated by Quigley (2012) based on Howie et al. (1990).

2.2.4 Necrotising enterocolitis in infants in neonatal units

The expected difference in costs of caring for infants below the age of one year for necrotising enterocolitis (NEC) following increases in breastfeeding/feeding with breastmilk are presented as potential cost-savings. The variety of alternative policy aims modelled with various hypothetical rates is shown in Table 2.4.

Table 2.4: Policy scenarios modelled for predicting the impact of increasing rate of breastmilk feeding on NEC for varying rates of 'any breastmilk feeding' at discharge within neonatal units

Definition of breastmilk feeding and rate used (2006) in base case	**Alternative policy scenarios modelled**		
Policy D0: Any breastmilk feeding rate at discharge from neonatal units (35%)	Policy D1: increase rate of any breastmilk feeding at discharge from neonatal units to 50%	Policy D2: increase rate of any breastmilk feeding at discharge from neonatal units to 75%	Policy D3: increase rate of any breastmilk feeding at discharge from neonatal units to 100%

The rate of 'any breastmilk feeding' used in the base case refers to 2006 data based on the study by Bonet et al (Bonet et al, 2010), a population based cohort of 3,006 very preterm births (22-31 weeks of gestation) discharged home from neonatal units in eight European countries including the UK. The Infant Feeding Survey 2005 rate was not considered relevant for this outcome because it refers to breastfeeding practice in all babies admitted to neonatal units at 1 and 2 weeks and not necessarily at discharge from the neonatal units. The babies at risk of NEC usually have a long stay in the neonatal unit and therefore it is important that breastfeeding rates at discharge are considered. Although the figures from Bonet et al refer to very pre-term babies admitted to neonatal units (rather than all babies admitted to neonatal units), the breastfeeding rates at discharge that they report are the only estimates available for the UK context. The modelled policy scenarios are hypothetical targets. The aim of Policy D1 is that half of all babies admitted to neonatal units are breastfed or receive breastmilk at discharge while the aim of Policy D2 increases this to three-quarters and Policy D3 increases this to all babies admitted to neonatal units being breastfed or receiving breastmilk at discharge.

The reference population was the total number of neonatal admissions (79,093), estimated as 10% of all live births in 2009 (790,938), sourced from the ONS (Office for National Statistics, 2010a). The choice of this group as the reference population was guided by the fact that whilst more breastmilk benefits all babies in the neonatal units, the falling rates of NEC will be seen among the subgroup most at risk (i.e. very preterm, very low birthweight babies who stay very long in the neonatal units). Two sources of data exist to support a rate of 10% of all newborn babies admitted to Neonatal Units. Macfarlane and Mugford (Macfarlane and Mugford, 2001) estimated the rate to be about 10% in all four countries of the UK using ONS data from 1995/96. Redshaw and Hamilton (Redshaw and Hamilton,

2006) estimated that there were a total of 74,510 neonatal admissions in the UK in 2005. The figures were based on "the responses to the surveys with additional information about admissions for non-respondents utilising the Directory of Critical Care". When compared with the total number of live births in that year, the rate is about 10%.

As breastmilk feeding rates increase in the neonatal units, fewer cases of NEC in babies would be expected. Only one type of health resource – the treatment of NEC during the stay in neonatal units - was considered.

The odds ratio of 0.19 (CI: 0.05-0.73) from Henderson et al (Henderson et al, 2009) was used to estimate impact on NEC treatment from breastfeeding. This OR referred to stage II/III NEC cases.

Incidence of NEC in the neonatal units (1 per 100 newborn babies) was estimated using Hospital Episode Statistics data (Information Centre for Health and Social Care, 2011). There were 677 finished consultant episodes recorded for ICD-10 disease code P77 (necrotising enterocolitis of fetus and newborn) in 2009-10 in England. The ONS population statistics for live births in that year is 671,058. Assuming 10% of this newborn population would have neonatal admissions (see above paragraph), 677 cases of NEC means an incidence rate of 1 per 100 newborn babies.

Costs of NEC treatment included two separate costs: costs of surgery for a proportion of all NEC cases admitted to the neonatal units and costs of stay (bed-day costs) in the neonatal units. Based on previous studies (Renfrew et al, 2010; Rice et al, 2010), the cost reported under HRG4 procedure, “major neonatal diagnosis (PB01Z)” was assumed to represent the cost of a NEC surgery. The unit cost of NEC surgery was derived as weighted average across long-, short- and excess bed-day stays, applying the same methodology as described in the gastroenteritis section. The results are given in Appendix 10 with the upper and lower quartile values used in the sensitivity analysis.

Based on a recent UK study on neonatal admissions, it was assumed that 31% of all NEC cases would have surgical intervention (Rees et al, 2010). Bed-day costs were estimated using the schedule 4 of NHS Reference Costs and applying the same methodology as above. HRG4 codes included were XA01-05Z (various procedures under ‘neonatal critical care’). The results are given in Appendix 10 with the upper and lower quartile values used in the sensitivity analysis.

Average length of stay in the neonatal unit for NEC cases was taken from Hospital Episode Statistics 2009-10 using primary diagnosis code P77 (necrotising enterocolitis of fetus and newborn) and was 26.7 days. Based on a previous study (Renfrew et al, 2010, Rice et al, 2010), it was assumed that the bed-day costs would cover hotel costs, therapy services, medical staff, ward consumables, blood and blood products, drugs, diagnostics, medical and surgical equipment and non-invasive positive pressure ventilation (theatre costs were excluded).

2.2.5 Maternal breast cancer

The expected differences in costs of caring for women with breast cancer following increases in breastfeeding are presented as potential cost-savings. The variety of alternative policy aims modelled is compared against varying definitions and rates achieved in 1996-2001 (Liu et al, 2009) in Table 2.5.

Table 2.5: Policy scenarios modelled against current practice for predicting the impact of increased breast feeding on maternal breast cancer

Definition of 'lifetime' breastfeeding and rate used (1996-2001) in base case	**Alternative policy scenarios modelled**		
Policy E0: 32% primiparous women never breastfeeding 36% breastfeeding for ≤6 months 16% breastfeeding for 7-18 months 16% breastfeeding for 18+months	Policy E1: Increase rate of breastfeeding for ≤6 months to 52% 16% never; 52% ≤6 months; 16% 7-18 months 16% 18+ months	Policy E2: Increase rate of breastfeeding for ≤ 18 months to 32% 16% never 36% ≤6 months 32% 7-18 months 16% 18+ months	Policy E3: Increase rate of breastfeeding for 18+ months to 32% 16% never 36% ≤6 months 16% 7-18 months 32% 18+ months

Information on the proportion of primiparous women who have breastfed for various durations (used for Policy E0) is taken from the Million Women Study (Liu et al, 2009). Unlike other outcomes used in this report, this outcome needs the duration of time the mother has breastfed for, rather than the amount of time the baby has fed for. Therefore, the breastfeeding rates given in the Infant Feeding Survey 2005 were not appropriate.

The alternative policy scenarios aim to reduce the number of women who never-breastfeed and increase the length of time for which women breastfeed over their lifetime. For example, Policy E1 aims at reducing the number of mothers who 'never breastfeed' by half (i.e. from 32% to 16%) and increasing the number of mothers who breastfeed for ≤6 months over their lifetime by 16 percentage points (i.e. from 36% to 52%). This translates to up to 3 months for each child (assuming average parity of two children per women) but would allow for the possibility of breastfeeding one child for up to 6 months and not breastfeeding a second child. Policy options E2 and E3 move the 16 percentage points to the number of mothers breastfeeding for 7-18 months and to greater than 18 months over their lifetime, while also reducing the number of mothers who 'never breastfeed' by half. Policy E2 and E3 can be achieved in more than one way: e.g. 'never breastfeeding' women start breastfeeding for>18months or alternatively for ≤6 months or longer, with women breastfeeding for ≤6 months also increasing to 7-18 months, and those breastfeeding for 7-18 months increasing to greater than 18 months.

Unlike the other four outcomes assessed in this study, breast cancer is a chronic condition and lasts beyond the first year of onset. Therefore, our analysis modelled follow-up of a cohort of primiparous women over their lifetime to predict how many would develop breast cancer and how many would die because of breast cancer or other causes over time. This

information was used to estimate average QALYs lost to breast cancer as well as average costs of treating a breast cancer over a lifetime from onset of breast cancer. The net present value of the average treatment costs and average QALYs lost to breast cancer were estimated for each policy scenario. To arrive at incremental benefit, a QALY was valued at £20,000 following NICE guidance. The incremental benefit is the difference in total loss (QALYs and treatment costs) between Policy E1 or E2 or E3 and Policy E0 (National Institute for Health and Clinical Excellence, 2008).
The odds ratios to identify women with breast cancer by feeding status were sourced from Beral et al (Collaborative Group on Hormonal Factors in Breast Cancer et al, 2002) and summarised in Table 2.6 below:

Table 2.6: Odds ratios and confidence intervals (CI) used to estimate the impact on breast cancer treatment from cumulative breastfeeding (over the lifetime of women), based on Beral et al (2002)

Breastfeeding definition	Mean	Lower CI	Upper CI
Ever breastfeeding vs. never breastfeeding	0.96	0.92	0.99
Breastfeeding for <6 months vs. never	0.98	0.95	1.01
Breastfeeding for 7-18 months vs. never	0.94	0.91	0.97
Breastfeeding for 18+ months vs. never*	0.89	0.84	0.94

*Assumed to be similar to odds ratio for 19-30 months reported in Beral et al. (OR=0.89). This OR is almost identical to the OR for 31-54 months (OR=0.88). Therefore, OR=0.89 is a reasonable estimation for 18+ months.

The lifetime risk of breast cancer (1 in 8) and age-specific 20-year relative survival were obtained from Cancer Research UK statistics (Cancer Research UK, 2011). The relative survival in any age group (e.g. 0.64 in 15-49 years) can be treated as a relative risk to adjust overall (all-cause) mortality in this age group, by multiplying overall mortality with (1/relative survival). If the overall mortality in the 15-49 years group is 0.0007, the annual probability of dying in this age group will be 0.00109 [0.0007 x (1 / 0.64)]. The mortality rates were sourced from the UK Life Tables (Office for National Statistics, 2010a).

Lifetime costs were discounted prior to averaging. Life years were adjusted by a utility value to estimate number of quality-adjusted life years (QALYs). The utility values used were: 0.71 (average), 0.80 (to represent lowest level of severity), 0.67 (to represent highest level of severity) (Robertson et al, 2011).

The unit cost of treating a breast cancer case was sourced from Dolan et al (Dolan et al, 1999) and inflated to 2009/10 prices (£11,726). The average cost of treating a Stage IV cancer (£16,260) was used as the higher end unit cost in the sensitivity analysis and was based on Remak and Brazil (Remak and Brazil, 2004). The discount rates used were 3.5% and 5% (for costs) and 3.5%, 1.5% and 5% for QALYs.

3. Methods of narrative economic analysis – shortlisted outcomes where modelling not possible

Three priority shortlisted outcomes were conditions where economic modelling was not appropriate or possible, either due to an absence of appropriate evidence, a limited understanding of the lifetime impacts of breastfeeding or simply the complexity that would be required to quantitatively estimate the financial impacts of breastfeeding. These were Sudden Infant Death Syndrome, cognitive outcomes, and childhood obesity. Furthermore, whilst health service impacts are associated with these conditions, it was recognised that they were also associated with significant non-health effects on the broader economy which would not have been reflected in our quantitative modelling approach. As a result, we chose to develop narrative commentaries to consider the financial impacts of these conditions and the potential benefits that might accrue as a result of changes in breastfeeding rates.

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Appendix 3

Databases searched and search strategies, for reviews A, B and C

Three separate searches were undertaken to identify studies for the following reviews

A. A review of existing systematic reviews of infant feeding and health/disease outcomes in developed/transitional countries.

B. A review of UK studies examining health outcomes related to infant feeding.

C. A review of the cost-of-illness associated with 'not-breastfeeding': examination of evidence reported from the UK and comparable industrialised countries**.**

The literature searches involved searching electronic databases covering health care, social care, and psychology. The database search strategies were devised to identify health outcomes related to breastfeeding and then included an additional facet of terms for each systematic review question: reviews, UK studies, and economic evaluations. This entailed combining subject indexing terms, such as MeSH in MEDLINE, and free text search terms in the title and abstract. The search terms were identified through discussion between the research team, by scanning background literature, and by browsing database thesauri. Methodological search filters were used in the review of reviews and review of economic evaluations. Searches for UK primary studies included a facet of terms to identify studies in the UK context through searches of the title, abstract, indexing, author address and other country-indicative fields. The searches were limited to English language in the systematic review of reviews, with non-English language studies downloaded separately. There were no date limits.

The following databases were searched:

- MEDLINE and MEDLINE In-process
- EMBASE
- Cochrane Database of Systematic Reviews (CDSR)
- CINAHL (Cumulative Index to Nursing & Allied Health)
- British Nursing Index (BNI)
- Science Citation Index (SCI)
- Conference Proceedings Citation Index-Science (CPCI-S)
- PsycINFO
- Maternity and Infant Care
- Sociological Abstracts
- Applied Social Science Index and Abstracts (ASSIA)
- Health Management Information Consortium (HMIC)
- LILACS (Latin American and Caribbean Center on Health Sciences)
- NHS Economic Evaluation Database (NHS EED)
- Health Economic Evaluations Database (HEED)
- Cost-Effectiveness Analysis (CEA) Registry
- RePEc (Research Papers in Economics)
- OAIster
- WHOLIS-WHO Library Catalogue

As a number of databases were searched, some degree of duplication resulted. In order to manage this issue, the titles and abstracts of bibliographic records were downloaded and imported into EndNote bibliographic management software and duplicate records removed.

MEDLINE Search Strategies

Due to the length of the search strategies, only the MEDLINE strategy is reproduced below. This strategy was translated and adapted to run in the other databases searched. The results, dates, date-ranges and interfaces used for all databases searched are listed in tables below. Full details of the search strategies are available on request from the authors.

A. A review of existing systematic reviews of infant feeding and health/disease outcomes in developed/transitional countries.

MEDLINE (OvidSP). 1950-2010/Aug week 5.

1 Breast Feeding/ (21785)
2 breastfe$.ti,ab. (10139)
3 (breast adj (fed$ or feed$)).ti,ab. (13026)
4 Lactation/ or Milk, Human/ (40847)
5 Milk Proteins/ (8012)
6 (breastmilk or lactation).ti,ab. (21551)
7 ((breast$1 or mother$1 or human or maternal) adj milk).ti,ab. (14032)
8 ((milk or breast$) adj1 express$).ti,ab. (644)
9 (breast pump$1 or breastpump$1).ti,ab. (168)
10 or/1-9 (77915)
11 Risk factors/ or Risk/ (507386)
12 Time factors/ (866781)
13 Age Factors/ (323738)
14 Case control studies/ (126792)
15 Prospective studies/ (286923)
16 Cohort studies/ (114302)
17 Follow-Up Studies/ (411882)
18 Cross-Sectional Studies/ (115945)
19 "Confounding Factors (Epidemiology)"/ (7373)
20 "Bias (Epidemiology)"/ (13853)
21 Models, Theoretical/ (80151)
22 Linear Models/ (36607)
23 Causality/ (10249)
24 Incidence/ or Prevalence/ (265858)
25 Mortality/ (30399)
26 Morbidity/ (20537)
27 Health Status/ (45864)
28 "Outcome Assessment (Health Care)"/ (37331)
29 Women's Health/ (17445)
30 exp Chronic Disease/ (193992)
31 Disease Susceptibility/ (20228)
32 Leukemia/ (45155)
33 Precursor Cell Lymphoblastic Leukemia-Lymphoma/ (16594)
34 Lymphoma, Non-Hodgkin/ (28131)
35 Hodgkin Disease/ (28600)
36 exp Cardiovascular Diseases/ (1592430)
37 exp Heart Diseases/ (762004)
38 Myocardial Ischemia/ (27997)
39 exp Vascular Diseases/ (1142013)
40 Blood Pressure/ (215207)

41 exp Cholesterol/ (119977)
42 Infection/ (27641)
43 exp Respiratory Tract Infections/ (249780)
44 Sepsis/ (36081)
45 exp Urinary Tract Infections/ (35093)
46 Rotavirus Infections/ (4796)
47 Haemophilus Infections/ (6281)
48 exp Otitis Media/ (19498)
49 exp Diabetes Mellitus, Type 2/ or diabetes mellitus/ (135769)
50 Blood Glucose/ (109659)
51 Hypoglycemia/ (18501)
52 Hyperlipidemias/ (21337)
53 Lipids/ (78144)
54 Metabolic Syndrome X/ (11451)
55 Obesity/ (93848)
56 Weight Gain/ (17737)
57 Weight Loss/ (17411)
58 Body Mass Index/ (53912)
59 Body Weight/ (144752)
60 Energy Metabolism/ (52822)
61 Appetite Regulation/ (1757)
62 exp Infant Nutrition Disorders/ (4188)
63 Child Nutrition Disorders/ (1953)
64 Child Nutritional Physiological Phenomena/ (6098)
65 Malnutrition/ (3899)
66 Micronutrients/ (2117)
67 Vitamin D Deficiency/ (5879)
68 Growth/ (23945)
69 Growth Disorders/ (12908)
70 Digestive System/ (21268)
71 Gastroenteritis/ (10560)
72 exp Inflammatory Bowel Diseases/ (49149)
73 exp Enterocolitis/ (8038)
74 Colitis, Ulcerative/ (23567)
75 Crohn Disease/ (25350)
76 Diarrhea/ (34110)
77 Helicobacter Infections/ (21231)
78 Helicobacter pylori/ (24712)
79 Celiac Disease/ (12814)
80 Intestinal Mucosa/ (53504)
81 Dermatitis, atopic/ (11956)
82 Asthma/ (90828)
83 Rhinitis, Allergic, Perennial/ (5605)
84 Immune System/ (10813)
85 Immune System Diseases/ (3193)
86 Immunity, Innate/ (23416)
87 Immunity, Mucosal/ (4359)
88 Immunity, Active/ (3231)
89 Antibody Formation/ (57135)
90 Autoimmune Diseases/ (37881)
91 Xenobiotics/ (4967)
92 Arthritis, Rheumatoid/ (72310)
93 Osteoporosis/ (29306)
94 Rickets/ (4690)
95 Dental Caries/ (32243)

96 exp Depressive Disorder/ (66734)
97 Depression/ (57311)
98 Stress, Psychological/ (67965)
99 exp Cognition Disorders/ (45152)
100 Intelligence/ (17812)
101 exp Mental Disorders Diagnosed in Childhood/ (121363)
102 Child Behavior Disorders/ or Behavior/ (40409)
103 exp Behavioral Symptoms/ (207630)
104 Attention Deficit Disorder with Hyperactivity/ (15112)
105 Birth Intervals/ (1236)
106 Immunization/ (39282)
107 Vaccination/ (46174)
108 Stroke/ (37487)
109 (health adj3 (outcome$ or benefit$1 or effect$1 or harm or harms or harmful or disbenefit$1)).ti,ab. (44435)
110 (protective adj3 (benefit$1 or effect$1 or outcome$ or impact$1)).ti,ab. (51150)
111 (harmful adj3 (effect$1 or outcome$ or impact$1)).ti,ab. (6394)
112 ((reduced or reduction$1 or fewer or less or lower) adj2 (risk or risks)).ti,ab. (36400)
113 ((longterm or long term) adj3 (benefit$1 or effect$1 or outcome$ or impact$1 or harm or harms or harmful or disbenefit$1)).ti,ab. (66386)
114 (chronic adj1 (disease$1 or illness$)).ti,ab. (31252)
115 (disease adj3 (predisposition or susceptibility)).ti,ab. (7499)
116 (breast$ adj3 (cancer$ or neoplasm$1 or tumo?r$1 or malignan$ or carcinoma$ or oncolog$ or sarcoma$ or adenocarcinoma$)).ti,ab. (159062)
117 (mamma$ adj3 (cancer$ or neoplasm$1 or tumo?r$1 or malignan$ or carcinoma$ or oncolog$ or sarcoma$ or adenocarcinoma$)).ti,ab. (23151)
118 (ovar$ adj3 (cancer$ or neoplasm$1 or tumo?r$1 or malignan$ or carcinoma$ or oncolog$ or sarcoma$ or adenocarcinoma$)).ti,ab. (46416)
119 ((colorectal or colo rectal) adj3 (cancer$ or neoplas$1 or oncolog$ or malignan$ or tumo?r$1 or carcinoma$ or adenocarcinoma$)).ti,ab. (51338)
120 ((colon or colonic) adj3 (cancer$ or neoplas$1 or oncolog$ or malignan$ or tumo?r$1 or carcinoma$ or adenocarcinoma$)).ti,ab. (46707)
121 ((rectal or rectum) adj3 (cancer$ or neoplas$1 or oncolog$ or malignan$ or tumo?r$1 or carcinoma$ or adenocarcinoma$)).ti,ab. (17890)
122 ((bowel$1 or large intestin$) adj3 (cancer$ or neoplas$1 or oncolog$ or malignan$ or tumo?r$1 or carcinoma$ or adenocarcinoma$)).ti,ab. (4848)
123 (bronch$ adj3 (cancer$ or neoplasm$1 or tumo?r$1 or malignan$ or carcinoma$ or oncolog$ or sarcoma$ or adenocarcinoma$)).ti,ab. (15239)
124 (endometr$ adj3 (cancer$ or neoplasm$1 or tumo?r$1 or malignan$ or carcinoma$ or oncolog$ or sarcoma$ or adenocarcinoma$)).ti,ab. (18898)
125 (gastrointest$ adj3 (cancer$ or neoplasm$1 or tumo?r$1 or malignan$ or carcinoma$ or oncolog$ or sarcoma$ or adenocarcinoma$)).ti,ab. (13224)
126 ((gyn?ecologic$ or urologic$ or genital$) adj3 (cancer$ or neoplasm$1 or tumo?r$1 or malignan$ or carcinoma$ or oncolog$ or sarcoma$ or adenocarcinoma$)).ti,ab. (13717)
127 ((child or children or childhood or infant$1) adj3 (cancer$ or neoplasm$1 or tumo?r$1 or malignan$ or carcinoma$ or oncolog$ or sarcoma$ or adenocarcinoma$)).ti,ab. (22410)
128 (cancer adj3 risk$1).ti,ab. (46559)
129 (leukemia or leukaemia).ti,ab. (157958)
130 (lymphoma$ adj3 non hodgkin$1).ti,ab. (25407)
131 ((lymphoma$ or disease) adj3 hodgkin$1).ti,ab. (43110)
132 ((cardiovascular or heart or vascular or cardiac) adj (disorder$1 or disease$1)).ti,ab. (192707)
133 (hypertens$ or blood pressure or BP).ti,ab. (439348)
134 (cholesterol$ or hypercholesterol$ or lipid level$1 or lipid profile$1).ti,ab. (161093)
135 infection$1.ti,ab. (739614)

136 (respiratory adj1 (disorder$1 or disease$1)).ti,ab. (16862)
137 (sepsis or septic$).ti,ab. (82331)
138 (urinary adj2 (disorder$1 or disease$1)).ti,ab. (2362)
139 rotavirus.ti,ab. (8266)
140 (haemophilus adj1 infection$1).ti,ab. (114)
141 (otitis media or (ear adj1 (inflammation or infection$1))).ti,ab. (14664)
142 (diabetes or diabetic).ti,ab. (293655)
143 ((blood adj1 glucose) or (blood adj1 sugar)).ti,ab. (38876)
144 (hypoglycemia or hypoglycaemia).ti,ab. (21849)
145 (hyperlip?emi$1 or lip?emi$1).ti,ab. (4351)
146 ((metabolic adj1 syndrome$1) or (insulin resistance adj1 syndrome$1)).ti,ab. (16243)
147 (adiposity or obesity or obese or overweight or weight gain or weight loss).ti,ab. (174747)
148 (body mass index or body weight or BMI).ti,ab. (186290)
149 ((appetite adj1 regulat$) or (food intake adj1 regulat$)).ti,ab. (1545)
150 (nutritional adj (disorder$1 or disease$1)).ti,ab. (727)
151 malnutrition.ti,ab. (21477)
152 micronutrients.ti,ab. (3210)
153 vitamin D deficien$.ti,ab. (3897)
154 child development.ti,ab. (2675)
155 (developmental disabilit$ or developmental delay$1).ti,ab. (7859)
156 (growth adj2 (child$ or infant$1 or adolesc$ or disorder$1 or retard$)).ti,ab. (24173)
157 (digestive adj1 (disorder$1 or disease$1)).ti,ab. (1841)
158 (bowel adj1 (disorder$1 or disease$1)).ti,ab. (20392)
159 (inflammatory adj (disorder$1 or disease$1)).ti,ab. (27957)
160 (intestinal adj (disorder$1 or disease$1)).ti,ab. (3279)
161 (diarrhoea$1 or diarrhea$1 or gastroenteritis).ti,ab. (69608)
162 (enterocolitis or colitis).ti,ab. (39934)
163 (crohn$2 disease$1 or ileocolitis or (terminal adj1 ileitis) or (regional adj1 ileitis)).ti,ab. (24072)
164 (granulomatous adj2 enteritis).ti,ab. (110)
165 (helicobacter pylori or campylobacter pylori).ti,ab. (25893)
166 (celiac or coeliac).ti,ab. (15775)
167 (intestinal adj1 mucosa).ti,ab. (9455)
168 (menstruation or polymenorrhea or hypomenorrhea or amenorrhea or dysmenorrhea or menorrhagia or oligomenorrhea or premenstrual syndrome or premenstrual tension).ti,ab. (18943)
169 (dermatitis or eczema or atopy).ti,ab. (44198)
170 (allergic or allergies or allergy).ti,ab. (97446)
171 asthma$.ti,ab. (96131)
172 rhinitis.ti,ab. (15190)
173 (sudden infant death$1 or cot death$1 or SIDS).ti,ab. (6002)
174 ((sudden unexplained death adj2 infancy) or SUDI).ti,ab. (49)
175 (bronchial adj (disorder$1 or disease$1)).ti,ab. (365)
176 (immune adj (disorder$1 or disease$1)).ti,ab. (2677)
177 (immunity or immunological).ti,ab. (170314)
178 (arthritis or arthritic).ti,ab. (103277)
179 (osteoporosis or osteoporoses).ti,ab. (33639)
180 (rickets or rachitis or rachitides).ti,ab. (4792)
181 dental caries.ti,ab. (10046)
182 ((depression or depressive or stress) adj3 (postpartum or post partum or postnatal or post natal or maternal or mother$1 or child$ or infant$1)).ti,ab. (9864)
183 ((cognition or cognitive) adj2 (disorder$1 or condition$1 or issue or issues or problem$1)).ti,ab. (4007)
184 (intelligence or intelligent).ti,ab. (18910)

185 ((behavio?r or behavio?ral) adj2 (disorder$1 or condition$1 or issue or issues or problem$1)).ti,ab. (16679)
186 (attention deficit$ or adhd).ti,ab. (13460)
187 hyperactiv$.ti,ab. (26872)
188 (birth adj1 (interval$1 or spacing)).ti,ab. (1249)
189 (vaccination or immuni?ation).ti,ab. (118453)
190 (stroke or strokes or cerebrovascular accident$1).ti,ab. (107968)
191 or/11-190 (7023026)
192 10 and 191 (41184)
193 exp Neoplasms/ and (Breast Feeding/ or breastfe$.ti,ab. or breast feed$.ti,ab. or breast fed$.ti,ab. or breastmilk.ti,ab. or breast milk.ti,ab.) (1102)
194 Child Development/ and (Breast Feeding/ or breastfe$.ti,ab. or breast feed$.ti,ab. or breast fed$.ti,ab. or breastmilk.ti,ab. or breast milk.ti,ab.) (833)
195 Developmental Disabilities/ and (Breast Feeding/ or breastfe$.ti,ab. or breast feed$.ti,ab. or breast fed$.ti,ab. or breastmilk.ti,ab. or breast milk.ti,ab.) (86)
196 Diarrhea, Infantile/ and (Breast Feeding/ or breastfe$.ti,ab. or breast feed$.ti,ab. or breast fed$.ti,ab. or breastmilk.ti,ab. or breast milk.ti,ab.) (561)
197 exp Menstruation Disturbances/ and (Breast Feeding/ or breastfe$.ti,ab. or breast feed$.ti,ab. or breast fed$.ti,ab. or breastmilk.ti,ab. or breast milk.ti,ab.) (391)
198 Menstruation/ and (Breast Feeding/ or breastfe$.ti,ab. or breast feed$.ti,ab. or breast fed$.ti,ab. or breastmilk.ti,ab. or breast milk.ti,ab.) (181)
199 Sudden Infant Death/ and (Breast Feeding/ or breastfe$.ti,ab. or breast feed$.ti,ab. or breast fed$.ti,ab. or breastmilk.ti,ab. or breast milk.ti,ab.) (273)
200 ((morbidity or mortality) adj3 (breastfe$ or breast feed$ or breast fed$ or breastmilk or breast milk)).ti,ab. (189)
201 or/193-200 (3423)
202 192 or 201 (41595)
203 review.ab. (470745)
204 review.pt. (1555271)
205 meta-analysis as topic/ (10618)
206 meta-analysis.ab. (20519)
207 meta-analysis.pt. (26121)
208 meta-analysis.ti. (13355)
209 or/203-208 (1749436)
210 (letter or editorial or comment).pt. (1021296)
211 animals/ not (animals/ and humans/) (3448922)
212 209 not (210 or 211) (1599029)
213 202 and 212 (5189)
214 limit 213 to english language (4481)
215 213 not 214 (708)

Reviews filter: Centre for Reviews and Dissemination (CRD). www.york.ac.uk/inst/crd/

B. A review of UK studies examining health outcomes related to infant feeding.

The search strategy for Review B replicates the first two facets of the search strategy for Review A: breastfeeding and health outcomes. The third facet of terms for reviews (line #209) was replaced by ‘United Kingdom’ specific search terms. This facet of search terms is reproduced below.

MEDLINE (OvidSP). 1950-2010/Sep week 2.

203 exp Great Britain/ (259370)

204 (united kingdom or britain or uk or england or wales or scotland or ireland or eire or british or english or scottish or welsh).ti,ab,in. (842910)
205 203 or 204 (1003009)
206 202 and 205 (2767)
207 (letter or editorial or comment).pt. (1023568)
208 animals/ not (animals/ and humans/) (3453344)
209 206 not (207 or 208) (2006)

C. A review of economic evaluations of infant feeding.

The search strategy for Review C replicates the first two facets of the search strategy for Review A: breastfeeding and outcomes. The third facet of terms for reviews (line #209) was replaced by the CRD economics search filter. This facet of search terms is reproduced below.

MEDLINE (OvidSP). 1950-2010/Sep week 2.

203 economics/ (25911)
204 exp "costs and cost analysis"/ (152705)
205 economics, dental/ (1834)
206 exp "economics, hospital"/ (16808)
207 economics, medical/ (8300)
208 economics, nursing/ (3823)
209 economics, pharmaceutical/ (2140)
210 (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).tw. (320092)
211 (expenditure$ not energy).tw. (13697)
212 (value adj1 money).tw. (16)
213 budget$.tw. (13871)
214 or/203-213 (430367)
215 ((energy or oxygen) adj cost).ti,ab. (2226)
216 (metabolic adj cost).ti,ab. (570)
217 ((energy or oxygen) adj expenditure).ti,ab. (12605)
218 or/215-217 (14806)
219 214 not 218 (426985)
220 202 and 219 (1892)
221 (letter or editorial or comment).pt. (1023568)
222 animals/ not (animals/ and humans/) (3453344)
223 220 not (221 or 222) (1461)

Search Results

Review A

Database	Interface/url	Date range	Search date	Results
MEDLINE and MEDLINE In-process	OvidSP	1950-2010/Aug week 5	10 Sep 2010	5,189 (60)
EMBASE	OvidSP	1980-2010/week 35	10 Sep 2010	6440
Cochrane Database of Systematic Reviews (CDSR)	Wiley interscience	2010:Issue 11	12 Nov 2010	74
CINAHL (Cumulative Index to Nursing & Allied Health)	EBSCO*host*	1982-2010/Sep week 1	14 Sep 2010	623
British Nursing Index (BNI)	OvidSP	1985-2010/Aug	14 Sep 2010	63
Science Citation Index (SCI)	Web of Science	1899-2010/Sep 11	14 Sep 2010	1,336
Conference Proceedings Citation Index-Science (CPCI-S)	Web of Science	1990-2010/Sep 11	14 Sep 2010	137
PsycINFO	OvidSP	1806-2010/Sep week 1	14 Sep 2010	612
Maternity and Infant care	OvidSP	1971-2010/Aug	14 Sep 2010	995
Sociological Abstracts	CSA Illumina	1952-2010/Aug	15 Sep 2010	26
Applied Social Science Index and Abstracts (ASSIA)	CSA Illumina	1987-2010/Aug	15 Sep 2010	19
Health Management Information Consortium (HMIC)	OvidSP	2010/July	15 Sep 2010	44
LILACS (Latin American and Caribbean Center on Health Sciences)	BIRME	1982-2010/Aug.	15 Sep 2010	78
OAIster	http://oaister.worldcat.org/		13 Oct 2010	94
WHOLIS-WHO Library Catalogue	http://dosei.who.int/uhtbin/webcat		13 Oct 2010	33
Total after de-duplication				11,090

Review B

Database	Interface/url	Date range	Search date	Results
MEDLINE and MEDLINE In-process	OvidSP	1950-2010/Sep week 2	27 Sep 2010	2,206 (44)
EMBASE	OvidSP	1980-2010/week 38	27 Sep 2010	2,070
CINAHL (Cumulative Index to Nursing & Allied Health)	EBSCO*host*	1982-2010/Sep week 2	27 Sep 2010	311
British Nursing Index (BNI)	OvidSP	1985-2010/Sep	27 Sep 2010	437
Science Citation Index (SCI)	Web of Science	1899-2010/Sep 25	27 Sep 2010	565
Conference Proceedings Citation Index-Science (CPCI-S)	Web of Science	1990-2010/Sep 25	27 Sep 2010	42
PsycINFO	OvidSP	1806-2010/Sep week 3	27 Sep 2010	270
Maternity and Infant care	OvidSP	1971-2010/Sep	28 Sep 2010	379
Sociological Abstracts	CSA Illumina	1952-2010/Aug	28 Sep 2010	44
Applied Social Science Index and Abstracts (ASSIA)	CSA Illumina	1987-2010/Aug	28 Sep 2010	34
Health Management Information Consortium (HMIC)	OvidSP	2010/Sep	28 Sep 2010	156
OAIster	http://oaister.worldcat.org/		13 Oct 2010	679
WHOLIS-WHO Library Catalogue	http://dosei.who.int/uhtbin/webcat		13 Oct 2010	10
Total after de-duplication				3,572

Review C

Database	Interface/url	Date range	Search date	Results
NHS Economic Evaluation Database (NHS EED)	CRD interface	2010/Sep 28	29 Sep 2010	116
Health Economic Evaluations Database (HEED)	Wiley interscience	2010/Aug	29 Sep 2010	101
MEDLINE and In-process	OvidSP	1950-2010/Sep week 2	29 Sep 2010	1,461 (38)
EMBASE	OvidSP	1980-2010/week 38	29 Sep 2010	933
CINAHL (Cumulative Index to Nursing & Allied Health)	EBSCO*host*	1982-2010/Sep week 3	29 Sep 2010	1,601
British Nursing Index (BNI)	OvidSP	1985-2010/Sep	29 Sep 2010	3
Science Citation Index (SCI)	Web of Science	1899-2010/Sep 25th	30 Sep 2010	737
Conference Proceedings Citation Index-Science (CPCI-S)	Web of Science	1990-2010/Sep 25	30 Sep 2010	62
PsycINFO	OvidSP	1806-2010/Sep week 3	30 Sep 2010	97
Maternity and Infant care	OvidSP	1971-2010/Sep	30 Sep 2010	294
Sociological Abstracts	CSA Illumina	Database unavailable	Database unavailable	Database unavailable
Applied Social Science Index and Abstracts (ASSIA)	CSA Illumina	1987-2010/Aug	30 Sep 2010	23
EconLit	OvidSP	1969-2010/Sep	30 Sep 2010	152
Health Management Information Consortium (HMIC)	OvidSP	2010/Sep	30 Sep 2010	34
CEA Registry	www.cearegistry.org	2010/Sep	30 Sep 2010	1
RePEc	http://ideas.repec.org	2010/Sep	30 Sep 2010	16
OAIster	http://oaister.worldcat.org/		13 Oct 2010	129
WHOLIS-WHO Library Catalogue	http://dosei.who.int/uhtbin/webcat		13 Oct 2010	10
Total after de-duplication				2,415

Appendix 4

Criteria used for initial screening of titles and abstracts: Reviews A, B and C

Review A: Systematic search and identification of existing reviews of infant feeding and health and cognitive outcomes in developed/transitional countries.

Topic: Health and cognitive outcomes of breastfeeding.

Design: Systematic review

At this stage, include abstracts that say they are reviews – we need to see the papers to decide which are not systematic reviews.

Participants: Developed/transitional countries

Only exclude on country if the title and abstract clearly state the review only included studies from developing/low income countries.

Intervention/Exposure: Breastfeeding

- to be included, some or all participants must be breastfeeding/feeding with breastmilk

At this stage do not exclude:

- systematic reviews of infants in intensive/special care baby units whose abstracts say they are comparing types of formula as there may be comparisons relevant to us
- systematic reviews of effects of medications for lactating mothers on mothers and infants.

Outcomes: Health and cognitive outcomes in relation to breastfeeding

Only exclude on outcomes if the title and abstract clearly state our outcomes were not examined.

Review B: Systematic search and identification of UK studies examining health outcomes related to infant feeding.

Topic: Health and cognitive outcomes of breastfeeding in the UK.

Design: Include relevant, controlled, experimental or epidemiological (observational or analytic) UK studies.

- as analytic studies, include two-group cross-sectional studies, case control studies, cohort studies
- include observational/ descriptive single-group cross-sectional or longitudinal studies that have some level of analysis
    - exclude case reports, case series, and papers that do not report a study.

Participants: To be included, must be in UK.

Intervention/ Exposure: Breastfeeding

- to be included, some or all participants must be breastfeeding/ feeding with breastmilk

Outcomes: Health and cognitive outcomes in relation to breastfeeding.

Only exclude on outcomes if the title and abstract clearly state our outcomes were not examined.

Review C: Systematic examination of evidence on the cost-of-illness associated with not breastfeeding reported from the UK and comparable industrialised countries.

Topic: Cost of illness associated with not breastfeeding.

Design: Cost of illness analyses.

Participants: UK and comparable industrialised countries.

Intervention/ Exposure: One of the following:

- breastfeeding/feeding with breast milk
- formula feeding.

Outcomes:

- Healthcare resource implications of treating conditions that could have been prevented by breastfeeding.
- Resource implications of other public services of meeting needs that could have been prevented by breastfeeding.

Appendix 5

The cost-of-illness associated with 'not-breastfeeding': a systematic examination of evidence reported from the UK and comparable industrialised countries

The search for this review is reported in Appendix 3 (Review C). The results of the searches are reported in Appendix 2, paragraph 1.4. Data extraction forms for the eleven included papers appear below, following description and appraisal of the papers, discussion and conclusions.

Of the 11 papers reviewed, 7 were reported from the US, 2 from Europe (Italy and the Netherlands) and 2 from Australia. The majority (7/11) were published in peer-reviewed journals as full-papers; 2 were summary reports in peer-reviewed journals and 2 were reports to government departments. All papers were published between 1997 and 2010. Of 9 papers that were published in peer-reviewed journals, 4 were published in paediatric journals.

Aims of the papers and definition of breastfeeding used:

Two distinct aims were reported: (a) 4/11 papers aimed at estimating 'averted' health care costs if current breastfeeding rates were to change to one or more hypothetical targets, one of which is usually the nation's National Breastfeeding Target (if it exists); and (b) 7/11 papers aimed at estimating 'excess' health care costs of 'not-breastfeeding' (i.e. formula feeding) infants or the 'attributable' costs of treating illnesses linked to artificial feeding. All papers assumed that breastfeeding (including donor milk) has a protective effect against adverse health outcomes (e.g. gastroenteritis or lower respiratory tract infections in infants- 8/11 papers) or health resource use (e.g. GP visits or hospitalisations regardless of being explicit on specific health outcomes- 3/11 papers). All 11 papers compared 'exclusive' breastfeeding at 3-6 months from birth (and during the stay in neonatal units, where applicable) with formula feeding. Two papers (Ball & Wright 1999; Smith et al. 2002) also compared 'any' breastfeeding with formula feeding.

Target population, sample size and inclusion/exclusion criteria

6/11 of the papers estimated health care costs for an entire population and 5/11 for a sample. The target population included: newborns of both genders (for child outcomes- 5/11), children between 0-4 years (Smith et al. 2002) and women (for breast and ovarian cancers – Buchner et al. 2008). The papers that based their analysis on samples included: infants (<1 year old) of both genders (4/11) and low birth weight babies of both genders (Wight 2001). Only one paper (Cattaneo et al. 2006) was explicit in terms of statistical power of their sample (80%). The papers were not always explicit about their inclusion and exclusion criteria: only 4/11 papers (Hoey & Ware 1997; Bartick & Reinhold 2010; Barton et al. 2001 and Smith et al. 2002) stated their exclusion criteria.

Cost perspectives

Although the cost perspectives were not explicitly stated in the reviewed papers, 3/11 took a societal perspective, 5/11 took a health care perspective, 2/11 took HMO (Health

Maintenance Organisation) perspective and 1/11 took a health insurer's perspective. The 3/11 papers that took societal perspectives included costs falling outside health sector (e.g. special education cost in Drane 1997), parental loss of time and wages while attending their children (Weimer 2001) or costs of premature deaths due to a condition likely to have caused by not breastfeeding (Bartick & Reinhold 2010; Weimer 2001).

Resource use: identification, measurement and valuation

The papers differed in terms of how resource use was identified, measured and valued. 10/11 papers included direct health care costs such as GP visits and hospitalisations and 1/10 (Barton et al. 2001) included direct variable costs and net revenue. About half (6/11) included the costs of treating conditions associated with formula-feeding relative to breastfeeding (Bartick & Reinhold 2010; Buchner et al. 2008; Drane 1997; Riordan 1997; Smith et al. 2002; Weimer 2001). These costs were identified as health resource use (e.g. GP visits or hospitalisations) specific to selected health outcomes (e.g. gastroenteritis), measured using annual incidence of those outcomes and valued by unit costs of treating the case in question. 3/11 papers identified health resource use (e.g. GP visits and hospitalisations without being explicit in the specific underlying causes for such resource use) in their study population, measured mean frequency of health service use per child, and valued the cost implications by unit cost (Ball & Wright 1999; Cattaneo et al. 2006; Hoey & Ware 1997). 2/11 papers identified the additional health care events and associated resource use that formula feeding or not using human milk would generate, measured mean events per formula-fed child and valued them using unit cost (Barton et al. 2001; Wight 2001).

A critical input parameter used in all studies was the incidence of disease (e.g. gastroenteritis) or incidence of care episode (e.g. GP visits or hospitalisations). 1/11 study (Buchner et al. 2008) generated incidence of disease using an epidemiological modelling; 6/11 used published literature or database (Ball & Wright 1999; Bartick & Reinhold 2010; Drane 1997; Riordan 1997; Smith et al. 2002; Weimer 2001); 1/11 obtained incidence data based on a study sample prospectively (Cattaneo et al. 2006); and 3/11 did so retrospectively (Barton et al. 2001, Hoey & Ware 1997; Wight 2001). Only 1/11 paper (Buchner et al. 2008) critically appraised the choice of parameter values by reviewing the evidence base systematically.

The final cost estimates were presented as 'averted costs' by increasing current breastfeeding rates to a hypothetical target (i.e. difference in total health care costs in breastfed and non-breastfed groups) in 4/11 papers and as 'excess health care costs' in non-breastfed group at the current breastfeeding rates in 6/11 papers. 1/11 paper presented 'attributable' hospital costs of treating illnesses for which breastfeeding is shown to be protective (Smith et al. 2002). The total cost-savings were obtained by adding up all cost-savings across all the outcomes included in the papers (10/11 papers).

The 3/11 studies that took a broader perspective (than health care only) included either the costs of premature deaths (Bartick & Reinhold 2010; Weimer 2001) by measuring the number of such deaths and valuing them using a labour-market approach (revealed preference model) or parental loss of time and wages by measuring parental time to look after their sick children and valuing the time by appropriate wage-rate (Weimer 2001) or

special educational needs of preterm children by measuring the incidence of special educational needs in children and valuing them by annual costs of such provision (Drane 1997).

Two of the eleven papers (Bartick & Reinhold 2010; Buchner 2008) included long-term outcomes- obesity and cancer. Buchner et al. (2008) is the only paper that included maternal outcomes (breast and ovarian cancers and rheumatoid arthritis). Both papers included obesity in their analysis. The costs were estimated for lifetime, first by measuring the annual incidence and then estimating the net present value (per annum) of treating such conditions. The net present value was obtained by discounting the future stream of costs.

Three of the eleven papers adjusted their cost estimates. The estimates were adjusted for maternal education level and maternal smoking status using ANOVA (Ball & Wright 1999); and for admissions, duration of breastfeeding, twin, and mother back to work in or after 4 months (Cattaneo et al. 2006). One of the eleven papers (Hoey & Ware 1997) did this adjustment partially as cost-savings were presented as weighted average based on well-sick visits, prescriptions and hospitalisations.

Health and non-health outcomes

Gastroenteritis (GI), otitis media (OM) and respiratory illnesses (RI) were the most common health-outcomes used (7/11). Necrotising enterocolitis (NEC) was included in 5/11 papers. Other childhood health-outcomes included were: atopic dermatitis (1/11), sudden infant death syndrome (1/11), childhood asthma (1/11); childhood leukaemia (2/11), diabetes (3/11), childhood obesity (2/11), eczema (3/11), Crohn's disease (1/11) and sepsis (1/11). One paper (Buchner et al. 2008) used maternal health-outcome: rheumatic arthritis, premenopausal breast cancer and ovarian cancer.

Time horizon and discounting of costs

All childhood health outcomes (except obesity in Bartick & Reinhold 2010 and Buchner et al. 2008) were modelled for one year, usually the first year of life although in Smith et al. (2002) the estimated annual costs of hospitalisation included hospital admissions in children aged 0-4 years. Bartick & Reinhold (2010) considered 40 years from birth (no justification provided) to model obesity while Buchner et al. (2008) considered lifetime as the appropriate time horizon to model obesity, maternal cancer and rheumatic arthritis. Only 4 papers (Ball & Wright 1999; Bartick & Reinhold 2010; Hoey & Ware 1997; Smith et al. 2002) explicitly stated the price year. Of 2 papers (Bartick & Reinhold 2010; Buchner et al. 2010) which estimated costs accruing beyond the first year of life, the discount rate chosen was between 3-5% following differing national guidelines.

Sensitivity analysis

Only 1/11 papers mentioned explicitly how they performed sensitivity analysis (Smith et al. 2002). However, one (Ball & Wright 1999) discussed the implications of findings for varied HMO costs. Another (Bartick & Reinhold 2010) occasionally mentioned more than one unit cost and used the lowest value, suggesting underestimation.

Reported economic impact

All papers reported positive economic impact of breastfeeding, i.e. increased breastfeeding is associated with potential cost-savings (Table 5.1). 6/11 papers reported the average impact per infant. They were: excess costs of US $331 per not-breastfed infant for a year (Ball & Wright 1999); mean difference of US $3,366 between breastfed and non-breastfed infants during neonatal unit stay for that year (Barton et al. 2001); a saving of Euro 250 per newborn per year on best case scenario of 100% breastfeeding for 6 months or more (Buchner et al. 2008); mean difference of Euro 160 per infant per year (Cattaneo et al. 2006); mean difference of US $200 per infant in the first 6-months of life; extra cost of US $9,669 per infant for not using human milk in a neonatal unit or a savings of US %11 per US $1 spent on human milk (Wight 2001).

Four of the eleven papers presented their findings in terms of potential savings if breastfeeding rates were to increase. There were: US $3.35 billion in treatment costs and US $13 billion including the value of premature deaths, at 90% breastfeeding rates (Bartick & Reinhold 2010); Australian $9 million in treatment costs and Australian $11.5 million including special education costs, at 80% breastfeeding rates (Drane 1997); between US $1.2 and 1.3 billion in treatment costs attributable to formula feeding (Riordan 1997); and US $0.5 billion in treatment costs and US $3.6 billion including the value of premature deaths, at 75% breastfeeding rate.

One paper presented 'attributable' hospital costs of treating illnesses for which breastfeeding is shown to be protective (Smith et al. 2002). This paper estimated a total of Australian $ 1.5 million in treating four diseases - gastrointestinal infections, respiratory illnesses, eczema, and NEC - in children aged 0-4 in Australian Capital Territory alone.

Table 5.1: Differences in healthcare costs of formula feeding vs. breastfeeding

Author/Date	Country	Definition of breastfeeding	Types of health outcomes	Time horizon	Population	Differences in total treatment costs	Differences in mean treatment costs
Ball & Wright (1999)	USA	Never breastfed; Partially breastfed (introduced formula in the first 3 months); Exclusive breastfed for ≥ 3 months	LRTI OM GI	From birth to 1 year	CRS sample= 1022 Dundee sample=617	Not reported.	$331 to $475 per never breastfed infant during the first year of life compared to EBF ≥ 3 months. Excess use per NB infant: 2.03 office visits 0.212 hospitalisations 0.609 prescriptions
Bartick & Reinhold (2010)	USA	Breastfed: CDC survey asked respondents if they had 'ever breast fed' Exclusive: Not	LRTI (+ deaths) OM GI NEC (+deaths) AD SIDS	Varies by condition Life span for death valuatio	2005 census data: 4.14 million live births and 80.8m people <20 years	$12.97 billion excess costs (including deaths) at 90% compliance and $10.49 billion at 80% compliance	

		having been fed anything other than breast milk Duration: Age when child 'completely' stopped being fed breast milk.	Childhood asthma (+deaths) Childhood leukaemia (+deaths) Type 1 diabetes (+ deaths) Childhood obesity	n not stated		$3.35 billion excess costs (excluding deaths) at 90% compliance	
Barton et al. (2001)	USA	Exclusive BF or exclusive formula feeding among NICU infants Source: retrospective audit of consultation logs	Weight gain during hospitalisation Length of stay Number of days infants received parental nutrition	October 1995-Jan 1996 but all work limited to in-patient stay in NICU	A non-random sample of 60 infants (39 in BF and 41 in formula)	None reported	Direct variable costs: $15179 (BF) $11813 (FF) Net revenue: $46,161 (BF) $35365 (FF) Both differences insignificant.
Buchner et al. (2008)	Holland	Exclusive breastfeeding or not Several scenarios compared with present situation	OM GI Asthma Respiratory infection Eczema Crohn's disease Leukaemia Obesity Rheumatic arthritis Premenopausal breast cancer Ovarian cancer	Lifetime from birth	187,910 infants born in 2005	Euro 50 million NPV per year if BF ≥ 6 months. A 5% shift from present situation will save Euro 4 million	Euro 20/newborn on a 5% shift. Euro 250/newborn on the best scenario (100% BF at 6+ months)
Cattaneo et al. (2006)	Italy	Exclusive breastfeeding at discharge and at 3 months; no breastfeeding at 3 months	No health outcomes specified	From birth to 1 year	A 80% powered sample of 842 newly born infants	Not reported	Euro 20.79 per additional month of BF (healthcare only) Euro 144.36 (healthcare + formula) Ambulatory: BF: Euro 34.69/infant CF/NBF=Euro 54.59/infant Hospital: BF: Euro 133.53/infant CF/NBF=Euro 254.03/infant

Drane (1997)	Australia	BF exclusively at 3 months vs. No breastfeeding	GI (term babies) NEC (pre-term and LBW) Eczema (LBW and term) IDDM	From birth to 1 year (health outcomes) Lifetime (special education)	Newly born infants Term=240000 Pre-term=16000	Pre-term infants: $ 6.56m Term infants: $4.69m IDDM=$523k Total: 11.5m NEC:$3.85m Eczema: $962k GI: $3.74m IDDM: $523k Special education: $2.69m	
Hoey & Ware (1997)	USA	Exclusive breastfeeding for at least 6 months vs. Exclusive formula-fed since birth (mixed feeding excluded)	Health resource use considered irrespective of illness	From birth to 12 months	A sample of 242 newly born infants out of 2140 for the HMO	BF = $900/infant Bottle= $1105/infant	$200/infant in favour of BF
Riordan (1997)	USA	Not always clear. For OM, it appears BF is exclusive at 4 months	Diarrhoeal diseases Respiratory syncytial virus (RSV) IDDM OM	Annual costs (From birth to 1 year)	Not clear. Diarrhoeal diseases= 16m episodes RSV=90,000 infants IDDM=120,000 children OM=not stated	GI/diarrhoea= $291.3m OM=$660m RSV=$225m IDDM=$9.6 - $124.8m Total = $1.19-$1.30b	
Smith et al. (2002	Australia	Exclusive breastfeeding (<6 mo, or >13 weeks); Breastfeeding (<14 weeks, <4 mo, <2 mo, <6 mo) Any breastfeeding	GI NEC LRTI OM Eczema	One year though children of ages 0-4 included	N=1193 women (93% of those who agreed to participate and were retained to six months postpartum.	Not reported. The total annual hospitalisation costs attributable to artificial feeding (5 conditions) = AUD 1,522,347 at 40% breastfeeding and AUD=1.2million at 60% breastfeeding	Not reported.
Weimer (2001)	USA	EBF at hospital discharge or at 5-6 months vs. No breastfeeding	OM NEC GI	From birth to 2 years Deaths (for all years)	3.9 million newly born infants in 1998; 291 LBW (for NEC)	OM=$2.786b GI=$72.59m NEC=$15.71b [Current BF rates (reference): OM & GI = 29% NEC=64%]	

Wight (2001)	USA	Use of donor milk vs. formula	Sepsis NEC	Not clear	140 very low birth weight infants	N/A	Total extra cost of not using human milk = $9669/infant Savings to NICU= $11 per $1 spent on human milk

Strengths and limitations of papers reviewed

One of the eleven papers (Bartick & Reinhold 2010) updated an earlier study (Weimer 2001) and proposed a formula to calculate disease/care episode incidence in breastfeeding and non-breastfeeding groups using the overall incidence of the disease/care episode. Another paper (Buchner et al. 2008) carried out a systematic review to choose the outcomes and based on the reported risk ratios, modelled the relative risks on their population. Three papers attempted to adjust their estimates for potential confounders (Ball & Wright 1999; Cattaneo et al. 2006; Hoey & Ware 1997). One paper (Drane 1997) included a cost-effectiveness analysis of breastfeeding in neonatal units. One paper (Smith et al. 2002) analysed the sensitivity of their estimated hospital costs of artificial feeding and presented alternative estimates according to different levels of effectiveness (relative risks) data.

Nine of the eleven papers did not critically discuss the choice of their two main input parameters- incidence of the disease (or care episode) and/or the unit costs of treating those diseases (or of the care episode). Only four studies reported the year to which their costs referred. 10/11 papers did not address the uncertainty around their point estimates of cost-savings or costs. The limitations of the studies were not sufficiently discussed. Where they were discussed (Bartick & Reinhold 2010; Weimer 2001), the discussions were related to the estimated cost-savings being an underestimation, rather than an overestimation - a claim that is hard to justify in the absence of relevant sensitivity analysis. However, one paper explicitly discussed the limitations of their approach and provided enough justification as to why some costs were overstated and some understated (Smith et al. 2002).

Discussion

Only four of the eleven papers reported the year to which their estimates referred. Therefore, it was not possible to compare the results directly across all studies. The other complications in terms of a meaningful comparison were that the estimated cost-savings referred to different breastfeeding scenarios in different countries; the number of health outcomes included in the studies differed significantly; and the definition of breastfeeding were not similar.

The reviewed papers provided some indication of the cost-of-illness associated with 'not-breastfeeding'. Despite huge variability across studies in terms of methods, the evidence indicates that increasing breastfeeding rates could lead to potential cost-savings to the NHS. The benefits may be wider and accrue in other areas, for example, education. However, there is a need to link potential costs savings to costs of programmes that would be needed to generate those savings. Without both costs and benefits evidence together, it would be hard to justify breastfeeding promotion policies on purely economic grounds. It is important

to note that scaling-up interventions may have differential cost-impact: increasing the current rate to the next realistic level (e.g. from 7% to 15%) may be much cheaper than increasing the rate from a higher level (e.g. 50% to 60%).

The most useful study was Bartick and Reinhold (2010) as this sets out clear methods to estimate the cost impact of 'not-breastfeeding'. However, the limitation of this study is the lack of critical appraisal of the quality of evidence used and exclusion of intervention costs. Future studies should therefore critically examine the evidence base on which their economic models are built and, to the extent possible, include the cost of interventions needed to increase the breastfeeding rates. They should also report all necessary aspects of their evaluation (e.g. choice of input parameters) to facilitate data synthesis in systematic reviews.

Conclusions

The papers reviewed varied significantly in terms of methods, breastfeeding rates, types of health resource used and disease conditions, making it impossible to compare the results in a meaningful way. Despite this variability, there is an indication that increasing current breastfeeding rates could lead to potential cost-savings to the NHS.

Data extraction form used for Review C (adapted from NICE 2006; CRD 2010; Drummond et al. 1996; Evers et al. 2005; and Chiou 2003)

General information		
Reviewer		
Date of extraction		
Weimer 2001dentifiers		
Endnote ID		
Author(s)/year of publication		
Title		
Type of publication		
Country of origin		
Barton et al. 2001 Characteristics	**Prompts to reviewer**	**Extracted data**
Aims and objectives	Clarity in: - research questions - perspectives - alternatives being considered	
Inclusion/exclusion criteria	Is this stated and clear?	
Population and/or sample size	Is whole population covered? If based on samples, what are implications for general population?	
Age/gender of participants	Is sub-group information provided and is important?	
Time horizon	Time horizon appropriate to include all costs (and effects)?	
Data and sources		
Exposure (breastfeeding)	Definition of breastfeeding and sources	
Health and other outcomes	All important health outcomes identified? Any other outcomes considered?	
Resource use	All relevant resource use identified and described?	
Statistical approach		
Measurement of health outcomes	What kind of events in each outcome (e.g. hospitalisation due to breast cancer) considered and measured?	
Measurement of resource use	What kind of resource use (e.g. GP visits, hospitalisation, and lifetime treatment) identified measured and valued?	

Discount rate	What is the discount rate applied (if any) and justification?	
Impact of breastfeeding	Is cost-saving projected for any increase in the prevalence, duration and exclusivity of breastfeeding? Is the methodology: - Incidence based? - Prevalence based? - Modelling? - Full cost of illness analysis - Use of attributable/preventable fractions?	
Uncertainty	Sensitivity analysis or other forms of uncertainty in estimates reported?	
Main findings		
Substantive results	- Costs of 'not breastfeeding'/'formula feeding' - by outcome category - by sub-group (if any) - indication of cost-savings	
Limitations		
Authors' indication	Implications for: generalisability of findings; over/under estimation of true costs/savings	
Reviewer's assessment	Conclusion based on findings? Robustness of methods and their implications for current UK study	

Data Table I: Study Identifiers

Endnote number	Author/Date	Citation
5/9	Ball & Wright (1999)	Ball TM, Wright AL. **Health care costs of formula-feeding in the first year of life**. Pediatrics 1999;103(4 Supplement S):870-876.
6/137	Bartick & Reinhold (2010)	Bartick M, Reinhold A. **The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis**. Pediatrics 2010;125(5):e1048-56.
7/65	Barton et al. (2001)	Barton AJ, Danek G, Owens B. **Clinical and economic outcomes of infants receiving breast milk in the NICU**. Journal of the Society of Pediatric Nurses 2001;6(1):5-10.
11/4118	Buchner et al. (2008)	Buchner FL, Hoekstra J, van Rossum CTM. **Health gain and economic evaluation of breastfeeding policies: Model simulation** (Gezondheidswinst en kosten-batenanalyse vaninterventies op het gebied van borstvoeding : Modelberekeningen): Rijksinstituut voor Volksgezondheid en Milieu RIVM; 2008
12/359	Cattaneo et al. (2006)	Cattaneo A, Ronfani L, Burmaz T, Quintero-Romero S, Macaluso A, Di Mario S. **Infant feeding and cost of health care: a cohort study**. Acta Paediatrica 2006;95(5):540-6.
14/96	Drane (1997)	Drane D. **Breastfeeding and formula feeding: a preliminary economic analysis**. Breastfeeding Review 1997;5(1):7-15.
19/97	Hoey & Ware (1997)	Hoey C, Ware JL. **Economic advantages of breast-feeding in an HMO setting: a pilot study. American Journal of Managed Care** 1997;3(6):861-865.
26/12	Riordan (1997)	Riordan JM. **The cost of not breastfeeding: a commentary**. Journal of Human Hypertension 1997;13(2):93-97.
32/7	Smith et al. (2002)	Smith JP, Thompson JF, Ellwood DA. **Hospital system costs of artificial infant feeding: estimates for the Australian Capital Territory**. Australian and New Zealand Journal of Public Health 2002;26(6):543-551.
36/3901	Weimer (2001)	Weimer J. **The economic benefits of breastfeeding: a review and analysis**. Food Assistance and Nutrition Research Report Number 13. Washington DC: US Department of Agriculture; 2001.
37/637	Wight (2001)	Wight NE. **Donor human milk for preterm infants**. Journal of Perinatology 2001;21(4):249-54.

Data Table II – Study characteristics

Paper	Publication	Reported country	Perspectives	Time horizon	Reported price year	Population covered
Ball & Wright (1999)	Peer reviewed journal article	USA	Payer/provider within a managed care system	From birth to 1 year	1995	CRS sample= 1022 (USA) Dundee sample=617 (Scotland)
Bartick & Reinhold (2010)	Peer reviewed journal article	USA	Societal	• Varies by condition • Life span for death valuation not stated	2007	2005 census data: 4.14 million live births and 80.8m people <20 years (USA)
Barton et al. (2001)	Peer reviewed journal article	USA	Health insurer	October 1995-Jan 1996 but all work limited to in-patient stay in NICU	Not specified	A non-random sample of 60 infants (39 in BF and 41 in formula) in a NICU (USA)
Buchner et al. (2008)	Report to Government department	Netherlands	Health care	Lifetime from birth	Not specified	187,910 infants born in 2005 (Netherlands)
Cattaneo et al. (2006)	Peer reviewed journal article	Italy	Not stated (implicit: health care)	From birth to 1 year	Not stated	A 80% powered sample of 842 newly born infants (50-152 per hospital) (Italy)
Drane (1997)	Peer reviewed journal article	Australia	Societal	From birth to 1 year (health outcomes) Lifetime (special education)	Not stated	Newly born infants Term=240000 Pre-term=16000 (Australia)
Hoey & Ware (1997)	Peer-reviewed journal article	USA	HMO	From birth to 12 months	1992-93	A sample of 242 newly born infants out of 2140 for the HMO (USA)
Riordan (1997)	Peer-reviewed journal article (summary paper)	USA	Health care	Annual costs (From birth to 1 year)	Not stated	Not clear. Diarrhoeal = 16m episodes RSV=90,000 infants IDDM=120,000 children OM=not stated (USA)

Smith et al. (2002)	Peer reviewed journal article	Australia	Health sector (hospital)	One year (children aged 0-4 years included)	1997/98	N=1193 women in Australian Capital Territory (93% of those who agreed to participate and were retained to six months postpartum.
Weimer (2001)	Report to Government department	USA	Societal	From birth to 2 years Deaths (for all years)	Not stated	3.9 million newly born infants in 1998; 291 LBW (for NEC) (USA)
Wight (2001)	Peer-reviewed journal article (summary report)	USA	NICU provider or health insurer	Not clear	Not stated	140 very low birth weight infants in a hospital (USA)

Data Table III: Aims of studies

Paper	Objectives	Inclusion/exclusion criteria	Author's stated limitations
Ball & Wright (1999)	To determine the excess cost of health care services for three illnesses in formula-fed infants in the first year of life, after adjusting for potential confounders.	1. Retrospective had to meet criteria of assessing the relationship between feeding status and infant illness 2. 2 samples used: a. CRS: Healthy infants using the paediatricians of a large local HMO. Infants were considered ineligible if they had used oxygen and/or ventilator after 6 hours of life or had had major congenital anomalies, any congenital problems of the chest or lung, symptomatic congenital heart disease, or any severe systemic disease. Families also were considered ineligible if they did not plan to continue their infant's care at the same clinic or did not speak English. [Used for LRI & OM] b. Dundee (Scotland) sample: Women with singleton pregnancies close to 36 weeks' gestation who lived in Dundee and were in a stable relationship were approached for participation. But = subsequent exclusion of 70 infants who delivered before 37 weeks, were ,2500 g, or stayed in the special care unit 48 hours, plus six infants whose mothers withdrew 3. Only costs accrued in the first year of life included because - the potential protective effects of breastfeeding are best documented for the first year of life - the current medical market demands a short-term return on each investment, such as perinatal breastfeeding promotion might require. Only direct medical care costs	Believe it is a conservative estimate of cost saving because: - some episodes of all three illnesses would be seen at more costly sites, such as urgent care centres or emergency rooms during hours when the paediatric offices were closed, - increases in the prevalence of resistant bacteria in OM that require more expensive - medications, as well as the trend to use small volume nebulizers in outpatient treatment of infants with LRI. - Costs for hospitalization also would be higher if the infant was admitted for intensive - care or if the plan is responsible for reimbursing the hospital for such ancillary fees as medications and procedures. - costs associated with other outcomes less common in breastfed infants in the first year, such as necrotizing enterocolitis and meningitis also have not been considered. - costs in Arizona are below the national average in both urban and rural settings Also note potential increases in costs of breastfeeding Some studies have shown that bilirubin levels are higher in breastfed infants, which might lead to increased hospitalization for jaundice. However, many of these studies included infants who were not breastfed adequately, and proper breastfeeding techniques have been shown to reduce jaundice substantially. BUT…. In a large study of illness visits and hospitalizations among 1829 Navajo infants born over a 2-year period, hospitalization for both dehydration and meningitis was significantly more common among never-breastfed infants, and jaundice was not significantly increased among breastfed infants, despite the predisposition among Native American infants to high bilirubin levels.

Bartick & Reinhold (2010)	Updated Weimer's estimate of economic impact of breastfeeding with more relevant data (accounting for exclusivity of breastfeeding and more recent estimates).	Excluded: costs of illnesses too mild to attend a Drs visit; adults deaths from asthma, type 1 diabetes, obesity, costs of childhood asthma that persist into adulthood and other adult disability. Definition of adult not clear (there is one reference to data up to 20yrs in the census). Additionally incidence data is given for different ages of children by disease is given but it is not clear if this is the totality considered.	Number of GI deaths too small to be reliable. Inconsistencies in some data especially around costs and breastfeeding durations
Barton et al. (2001)	Comparison of clinical and economic outcomes of infants who received their mothers' breast milk while they were in NICU compared with those who did not.	Inclusion criteria (a) infants born at the hospital, (b) infants discharged to home from the hospital, and (c) infants exclusively fed either breast *milk* or formula.	Small sample size There might be some length of stay differences in a larger sample (with breastfed babies staying longer to establish weight gain but it wasn't statistically significantly different.
Buchner et al. (2008)	To establish health effects and health care costs of new policy targets on breastfeeding Second unstated aim is CE of the breastfeeding 'masterplan' and 'baby friendly hospital initiative'	Assessment predicted for Dutch general population. Authors noted "health effects under certain specific conditions were not taken into account, such as extreme exposure to environmental chemicals, hepatitis C, HIV/AIDS, illicit drug use, implants and breast surgery, metabolic disorders, or use of drugs such as anti-anxiety or anti-depressant." Noted did not include costs outside health sector	• Limited in health outcomes that could be included • Assumed associations between breastfeeding and health outcomes found in other developed countries are valid for the general Dutch population • residual confounding for the association between breastfeeding and health outcomes is limited • Association of breastfeeding with disease may be overestimated due to publication bias • No distinction made between exclusive and partial breastfeeding • DALYs are controversial especially for minor illnesses • No productivity costs included • Health care costs of obesity not included
Cattaneo et al. (2006)	Aims to consider the use and costs of health care for groups of infants with difference feeding patterns.	Excluded pre-term infants	Exclusion of pre-term and sick infants. Unavailability of costs for some resource use items. Exclusion of indirect costs. Time horizon limited to 12 months. Note: Weimer 2001 identifies association not causality and it is impossible to exclude the effects of reverse causality. Identify recall bias and potential for misclassification of breastfeeding

Drane (1997)	Estimate cost savings from an increase in national prevalence of bf Examine other sources of economic evidence on bf Conduct a basis cost utility analysis Highlight areas for further research	Not clearly stated. General population analysis	Recognised as an underestimation as the analysis is partial, taking into account only the costs associated with hospitalisation.
Hoey & Ware (1997)	Retrospective chart review to identify resource use in the first year of life, according to feeding status. Positioned as a pilot study to determine whether retrospective chart review is an appropriate design.	Excluded premature births, multiple gestation, or newborns with a prolonged length of stay	Recognised as a pilot study. Design was small, demographic factors were not controlled and clinical severity of office visits was unrecorded.
Riordan (1997)	Research questions are not clearly stated at the outset nor are the perspectives of the analysis. The considers the costs of breastfeeding vs. no breastfeeding, for a small number of conditions known to be associated with bf	Not stated	Lack of reliable epidemiological data means
Smith et al. (2002)	To estimate for the Australian Capital Territory (ACT) the attributable hospital system costs of treating illnesses for which breastfeeding is established to be protective.	4. Included: women aged >=16 years and gave birth to a live baby between March and October 1997 in any of the ACTs two public hospitals, two private hospitals or at home. 5. Excluded: women whose babies were admitted to the neonatal intensive care unit or adopted and women who were critically ill, unable to give informed consent or complete the questionnaires for any reason or were participating in any other study.	No individual level matching of hospitalisation and risk exposure data was possible (hence population-level matching). The breastfeeding rates are derived from the cohort study (population survey) and are assumed to apply in the children who were admitted to the hospital (hospital episode data). This means factors other than feeding patterns cannot be excluded as factors contributing to hospitalisation. This study therefore may have understated the attributable costs. To aid a discussion on this, attributable costs are estimated for various exposure rates. Other study parameters that may have understated attributable costs: breastfeeding rates, lack of precision in categorising

			breastfed vs. formula-fed babies, pooled risk estimates for 4 conditions other than NEC where attributable costs may have been overstated as the prevalence of human milk feeding by premature infants was assumed to be the same as for term babies.
Weimer (2001)	To document the cost savings that would occur if nationwide prevalence of exclusive breastfeeding either at hospital discharge or at 5-6 months increased from present levels (1998: 29% breastfed at 6 months, 64% on discharge from hospital) to that recommended by the Surgeon General (≥50% breastfed at 6 months, ≥75% on discharge from hospital)	Costs limited to short term easier to measure costs Outcomes limited to 3 disease/conditions I year of births in US	Only 3 diseases studied Excludes costs spent on over the counter drugs for treatment of OM and gastroenteritis as well as physician charges related to the treatment of NEC, and cost savings due to reductions in long term morbidity Notes future studies should consider: rates of hospitalization, duration of hospitalization, health-service use, and medical costs among breastfed and formula-fed infants. Queries breastfeeding rates based on a formula feed company data
Wight (2001)	To document the extent to which human milk benefit preterm infants	Only pre-term babies included	Authors do not discuss the limitations of their methods and implications.

Data Table IV: Definitions

Paper	Definition of breastfeeding	Types of health outcomes	Types of health resource use	Discount rate	Sensitivity analysis carried out (Yes/No)	Data sources
Ball & Wright (1999)	• Never breastfed • Partially breastfed (introduced formula in the first 3 months) • Exclusive breastfed for ≥ 3 months	• LRTI • OM • GI	Mean number office visits Follow up visits Medications Chest radiography Hospitalisation	Not applicable	Varied HMO costs	LRI: Occurrence of LRI in the first 3 years of life from forms completed by the physician at the time of an acute episode. OM: The medical records of children in the study were reviewed when children were 3 years old for episodes of OM diagnosed during well-child and sick-child visits GI: Health visitors reported new episodes of GI. A medical record review was conducted to confirm illnesses for which care was obtained
Bartick & Reinhold (2010)	• Breastfed: CDC survey asked respondents if they had 'ever breast fed' • Exclusive: Not having been fed anything other than breast milk • Duration: Age when child 'completely' stopped being fed breast milk.	• LRTI (+ deaths) • OM • GI • NEC (+deaths) • AD • SIDS • Childhood asthma (+deaths) • Childhood leukaemia (+deaths) • Type 1 diabetes (+ deaths) • Childhood obesity	OPD visits Hospitalisations Medical and surgical treatment	3% considered inflation free	No. Occasionally two costs considered and lower used	AHRQ report on outcomes Hospitalisation rates, average length of stay and treatment length assumptions comes from various published sources.

Barton et al. (2001)	Exclusive BF or exclusive formula feeding among NICU infants Source: retrospective audit of consultation logs	• Weight gain during hospitalisation • Length of stay • Number of days infants received parental nutrition	Direct variable costs and net revenue (charge rather than cost-based estimates)	Not applicable	No	• Resource demand scale (not described) • Direct variable costs based on patient charges for supplies and equipment used during hospitalisations • Net revenue was based on the difference between reimbursement received
Buchner et al. (2008)	Exclusive breastfeeding or not Several scenarios compared with present situation	• OM • GI • Asthma • Respiratory infection • Eczema • Crohn's disease • Leukaemia • Obesity • Rheumatic arthritis • Premenopausal breast cancer • Ovarian cancer	Diagnostic and treatment costs of: • GP consultations • Admissions • Prescriptions • Lab research	4% according to Dutch guidelines	No with any individual scenario	2006 RIIVM Report Cost of diseases plus assumptions
Cattaneo et al. (2006)	Exclusive breastfeeding at discharge and at 3 months; no breastfeeding at 3 months	No health outcomes specified	• NHS and private paediatrician visits • Hospital OPD and A&E visits • Mother/child clinic visits • Admissions	Not applicable	No	• Prospective self-reports of health service use • Case payments (admissions) • Listed price (drugs)
Drane (1997)	BF exclusively at 3 months vs. No breastfeeding	GI (term babies) NEC (pre-term and LBW) Eczema (LBW and term) IDDM	• Hospitalisations (with or without surgeries) • GP visits • OPD attendances	5% where appropriate	No	• DRG/case payments • Published literature

Hoey & Ware (1997)	Exclusive breastfeeding for at least 6 months vs. Exclusive formula-fed since birth (mixed feeding excluded)	Health resource use considered irrespective of illness	• Routine office visits • Sick office visits • Hospitalisations • Drugs	Not applicable	No	Retrospective chart review Fee-for-service scale for office visits Actual costs for prescriptions and hospitalisations
Riordan (1997)	Not always clear. For OM, it appears BF is exclusive at 4 months	• Diarrhoeal diseases • Respiratory syncytial virus (RSV) • IDDM • OM	• Ambulatory • Hospitalisations • treatment costs/child derived from earlier studies	Not specified	No	Derived from various published sources.
Smith et al. (2002)	• Exclusive breastfeeding (<6 mo, or >13 weeks) • Breastfeeding (<14 weeks, <4 mo, <2 mo, <6 mo) • Any breastfeeding	• GI • NEC • LRTI • OM • Eczema	Number of episodes of hospitalisation	Not reported	Varied exposure rates and relative risks	ACT Population cohort study National Hospital Cost Data Collection (NHCDC) Relative risks based on literature search
Weimer (2001)	EBF at hospital discharge or at 5-6 months vs. No breastfeeding	• OM • NEC • GI	• Physician office visits • Lab research • Admissions • Time lost to parents of attending children	Not specified	No	• AHCPR cost analyses • Published sources • Assumptions
Wight (2001)	Use of donor milk vs. formula	• Sepsis • NEC	• Hospitalisation • Drugs • Diagnostic procedures • Lab research	Not specified	No	Unit costs and length of stay derived from a single NICU

Data Table V: Costs included in studies

Paper	Direct costs	Indirect costs	Methods used to estimate impact	Definition of impact	Estimates adjusted for covariates (Yes/No)
Ball & Wright (1999)	Consultations Procedures Prescriptions Hospitalisations	Not included	Incidence-based modelling based on observed events	**Cost saving** projected for exclusive BF over formula. Savings occur due to mean difference in mean frequency of use per child	Yes • Maternal education level • Maternal smoking In the first year of live using ANOVA
Bartick & Reinhold (2010)	Outpatient visits Hospitalisation Medical treatment (per case) Surgical treatment (per case)	Costs associated with age- and time-adjusted death	Incidence-based modelling based on two different breastfeeding scenarios	**Cost saving** projected as the difference in costs of treating conditions among breastfed children and formula fed children at current and target (80-90% EBF at 6 months). Value of life/death is based on labour market approach ($10.56m).	No
Barton et al. (2001)	Patient charges; Reimbursement	Not included	Incidence based comparison of variable costs between BF and formula fed NICU infants	Difference in variable costs and net revenue between BF and formula fed NICU infants	No
Buchner et al. (2008)	Consultations Admissions Procedures Prescriptions	Not included	Model-based incidence generated and costed using a formula for 8 different scenarios	Savings on health care costs by different scenarios compared to present situation	No
Cattaneo et al. (2006)	NHS and private paediatrician visits Hospital OPD and A&E visits Mother/child clinic visits Admissions	Not included	Prospective collection of health resource use data for 12 months from the sampled mothers/babies	Difference in health care costs in the first year of life between fully breastfed and not fully breastfed infants	Yes *Admissions, duration to breastfeeding, twin, mother back to work in or after 4 months

Drane (1997)	Hospital admissions Surgical procedures GP visits OPD attendances	Lifetime special education costs	Incidence-based estimates. Derives 'attributable risk percentage' to calculate number of cases in formula fed infants	Cost-savings as difference in costs of treatment between children at current (60%) BF rates and target (80%) BF rates. Also makes crude attempt to estimate Cost/QALY due to increase in BF rates	No
Hoey & Ware (1997)	Office visits (routine + sick) Drugs Hospitalisations	Not included	Incidence-based estimates	Cost-savings resulting from exclusive breastfeeding for 6 months compared to exclusive bottle-feeding during first year of life	Partially, as average presented as weighted based on total costs of well/sick visits, prescriptions and hospitalisations
Riordan (1997)	Hospitalisations GP visits	Lost productivity (missed work) associated with included conditions	Incidence-based data synthesis. Uses 'quasi' attributable fractions by attempting to identify the proportion of cases attributable to not BF based on estimates from previous literature.	Costs of 'not breastfeeding' as treatment costs attributable to formula feeding	No
Smith et al. (2002)	Hospital costs (includes direct and overhead costs)	Not included	Prevalence based population attributable fraction	**Costs attributable to artificial infant feeding** estimated for five conditions examined.	Yes. Relative risks taken are adjusted for important covariates.
Weimer (2001)	Consultations Lab procedures Admissions	Time lost to attending children Lost life due to disease	Incidence-based estimates	Cost-savings by increasing current BF prevalence rates to hypothetical targets	No
Wight (2001)	Hospitalisation broken into nursing care, diagnostic procedures and lab research	None	Incidence-based estimates derived from a single NICU on a sample of VLBW infants	Cost of not using human milk as the extra health resource use by those infants who did not use human milk	No

Data Table VI: Differences in healthcare costs of formula feeding vs. breastfeeding

Paper	Country	Time horizon	Population	Differences in total treatment costs	Differences in mean treatment costs
Ball & Wright (1999)	USA	From birth to 1 year	CRS sample= 1022 Dundee sample=617	Not reported.	$331 to $475 per never breastfed infant during the first year of life compared to EBF ≥ 3 months. Excess use per NB infant: 2.03 office visits 0.212 hospitalisations 0.609 prescriptions
Bartick & Reinhold (2010)	USA	• Varies by condition • Life span for death valuation not stated	2005 census data: 4.14 million live births and 80.8m people <20 years	$12.97 billion excess costs (including deaths) at 90% compliance and $10.49 billion at 80% compliance $3.35 billion excess costs (excluding deaths) at 90% compliance	
Barton et al. (2001)	USA	October 1995-Jan 1996 but all work limited to in-patient stay in NICU	A non-random sample of 60 infants (39 in BF and 41 in formula)	None reported	Direct variable costs: $15179 (BF) $11813 (FF) Net revenue: $46,161 (BF) $35365 (FF) Both differences insignificant.
Buchner et al. (2008)	Netherlands	Lifetime from birth	187,910 infants born in 2005	Euro 50 million NPV per year if BF ≥ 6 months. A 5% shift from present situation will save Euro 4 million	Euro 20/newborn on a 5% shift. Euro 250/newborn on the best scenario (100% BF at 6+ months)
Cattaneo et al. (2006)	Italy	From birth to 1 year	A 80% powered sample of 842 newly born infants	Not reported	Euro 20.79 per additional month of BF (healthcare only) Euro 144.36 (healthcare + formula) Ambulatory: BF: Euro 34.69/infant CF/NBF=Euro 54.59/infant

					Hospital: BF: Euro 133.53/infant CF/NBF=Euro 254.03/infant
Drane (1997)	Australia	From birth to 1 year (health outcomes) Lifetime (special education)	Newly born infants Term=240000 Pre-term=16000	Pre-term infants: $ 6.56m Term infants: $4.69m IDDM=$523k Total: 11.5m NEC:$3.85m Eczema: $962k GI: $3.74m IDDM: $523k Special education: $2.69m	
Hoey & Ware (1997)	USA	From birth to 12 months	A sample of 242 newly born infants out of 2140 for the HMO	BF = $900/infant Bottle= $1105/infant	$200/infant in favour of BF
Riordan (1997)	USA	Annual costs (From birth to 1 year)	Not clear. Diarrhoeal diseases= 16m episodes RSV=90,000 infants IDDM=120,000 children OM=not stated	GI/diarrhoea= $291.3m OM=$660m RSV=$225m IDDM=$9.6 - $124.8m Total = $1.19-$1.30b	
Smith et al. (2002)	Australia	One year though children aged 0-4 years included	N=1193 women in Australian Capital Territory (93% of those who agreed to participate and were retained to six months postpartum.	Not reported. The total annual hospitalisation costs attributable to artificial feeding (5 conditions) = AUD 1,522,347 at 40% breastfeeding and AUD=1.2million at 60% breastfeeding	Not reported.

Weimer (2001)	USA	From birth to 2 years Deaths (for all years)	3.9 million newly born infants in 1998; 291 LBW (for NEC)	OM=$2.786b GI=$72.59m NEC=$15.71b [Current BF rates (reference): OM & GI = 29% NEC=64%]	
Wight (2001)	USA	Not clear	140 very low birth weight infants	N/A	Total extra cost of not using human milk = $9669/infant Savings to NICU= $11 per $1 spent on human milk

Data Table VII: Other costs of formula feeding vs. breastfeeding

Paper	Country	Time horizon	Population	Total other differential costs	Mean other differential costs	Remarks
Ball & Wright (1999)	USA	From birth to 1 year	CRS sample= 1022 Dundee sample=617	None	None	No other costs included in analysis
Bartick & Reinhold (2010)	USA	• Varies by condition • Life span for death valuation not stated	2005 census data: 4.14 million live births and 80.8m people <20 years	911 excess deaths with 90% compliance and 741 with 80% compliance	(estimated by SP)	Indirect costs: Labour market approach to value a life at $10.56m per death
Barton et al. (2001)	USA	October 1995-Jan 1996 but all work limited to in-patient stay in NICU	A non-random sample of 60 infants (39 in BF and 41 in formula)	None	N/A	
Buchner et al. (2008)	Netherlands	Lifetime from birth	187,910 infants born in 2005		-25 DALYs/1000 newborn (best case)	
Cattaneo et al. (2006)	Italy	From birth to 1 year	A 80% powered sample of 842 newly born infants	None	None	
Drane (1997)	Australia	From birth to 1 year (health outcomes) Lifetime (special education)	Newly born infants Term=240000 Pre-term=16000	Special educational costs (pre-term babies) $2.69m		
Hoey & Ware (1997)	USA	From birth to 12 months	A sample of 242 newly born infants out of 2140 for the HMO	None	None	
Riordan (1997)	USA	Annual costs (From birth to 1 year)	Not clear. Diarrhoeal diseases= 16m episodes RSV=90,000 infants IDDM=120,000 children OM=not stated	None reported	None reported	

Smith et al. (2002)	Australia	One year though children aged 0-4 years included	N=1193 women in Australian Capital Territory (93% of those who agreed to participate and were retained to six months postpartum.	None	None	No other costs included in analysis
Weimer (2001)	USA	From birth to 2 years Deaths (for all years)	3.9 million newly born infants in 1998; 291 LBW (for NEC)	Parental loss of time and wages: $1.14m Value of premature deaths: $3.16b		
Wight (2001)	USA	Not clear	140 very low birth weight infants	N/A	N/A	

Data Table VIII: Healthcare costs of formula feeding vs. breastfeeding by disease area and location of care

Paper	Country	Time horizon	Population	Differential treatment costs by disease area	Differential Treatment Costs by location of care	Mean differential treatment costs
Ball & Wright (1999)	USA	From birth to 1 year	CRS sample= 1022 Dundee sample=617	Partially reported. Unit is per NBF infant. Medication LRI: $0.11 Medication OM: $7.57 Hospitalisation LRI: $26.59 Hospitalisation GI: $161.28	Primary care: $143 Secondary care: $188 Unit is per NBF infant	Primary care: $143 Secondary care: $188 Total: $331 Unit is per NBF infant
Bartick & Reinhold (2010)	USA	• Varies by condition • Life span for death valuation not stated	2005 census data: 4.14 million live births and 80.8m people <20 years	Excess costs with 90% compliance ($) ex. deaths: OM: 909m AD:601m Obesity= 592m LRTI=451m Asthma=335m NEC=267m GI=186m Type 1 diabetes=8.4m Leukaemia=1.98m	Only reported for LRTI: Secondary care: LRTI hospitalisation excess cost at 90% compliance=$451m At 80% compliance=$382m	
Barton et al. (2001)	USA	October 1995-Jan 1996 but all work limited to in-patient stay in NICU	A non-random sample of 60 infants (39 in BF and 41 in formula)	N/A	Secondary care: Hospitalisation at NICU Direct variable costs: $15179 (BF) $11813 (FF) Net revenue: $46,161 (BF) $35365 (FF) Both differences insignificant.	Direct variable costs: $15179 (BF) $11813 (FF) Net revenue: $46,161 (BF) $35365 (FF)

Buchner et al. (2008)	Netherlands	Lifetime from birth	187,910 infants born in 2005	N/A	N/A	Euro -250/newborn at best case scenario
Cattaneo et al. (2006)	Italy	From birth to 1 year	A 80% powered sample of 842 newly born infants	N/A	Euro 20.79 per additional month of BF (healthcare only) Euro 144.36 (healthcare + formula) Ambulatory: BF: Euro 34.69/infant CF/NBF=Euro 54.59/infant Hospital: BF: Euro 133.53/infant CF/NBF=Euro 254.03/infant	
Drane (1997)	Australia	From birth to 1 year (health outcomes) Lifetime (special education)	Newly born infants Term=240000 Pre-term=16000	Pre-term infants: $ 6.56m Term infants: $4.69m IDDM=$523k Total: 11.5m NEC:$3.85m Eczema: $962k GI: $3.74m IDDM: $523k Special education: $2.69m	N/A	
Hoey & Ware (1997)	USA	From birth to 12 months	A sample of 242 newly born infants out of 2140 for the HMO	N/A	Primary: $770 (BF), $ 823 (bottle) Secondary: $133 (BF), $282 (bottle)	

Riordan (1997)	USA	Annual costs (From birth to 1 year)	Not clear. Diarrhoeal diseases= 16m episodes RSV=90,000 infants IDDM=120,000 children OM=not stated	GI/diarrhoea= $291.3m OM=$660m RSV=$225m IDDM=$9.6 - $124.8m Total = $1.19-$1.30b	Primary: Diarrhoea- $133m Secondary: Diarrhoea- $158m RSV- $225m Others- not specified.	
Smith et al. (2002)	Australia	One year, though children 0-4 years of age included	N=1193 women in Australian Capital Territory (93% of those who agreed to participate and were retained to six months postpartum.	Hospitalisation costs (AUD) GI= 492,667 AOM= 198,953 Respiratory = 730,132 Eczema = 3,910 NEC= 96,686 Total = 1,522,347	All reported costs are hospital costs	Not reported
Weimer (2001)	USA	From birth to 2 years Deaths (for all years)	3.9 million newly born infants in 1998; 291 LBW (for NEC)	OM=$2.786b GI=$72.59m NEC=$15.71b	N/A	
Wight (2001)	USA	Not clear	140 very low birth weight infants		Total extra cost of not using human milk = $9669/infant Savings to NICU= $11 per $1 spent on human milk	

Data Table IX: Economic impact of breastfeeding

Paper	Country	Time horizon	Population	Economic impact defined by	Total economic impact	Mean economic impact (£)	Limitations
Ball & Wright (1999)	USA	From birth to 1 year	CRS sample= 1022 Dundee sample=617	Mean difference in average costs of treating a never-breastfed infant and a EBF (≥ 3 months) infant in the first year of life	Not reported	Primary care: $143 Secondary care: $188 Total: $331 Unit is per NBF infant	• Only 3 outcomes examined • Savings not projected for exclusive vs. partial BF • Savings might have been overestimated in the absence of right statistical approach • No distribution of means considered
Bartick & Reinhold (2010)	USA	• Varies by condition • Life span for death valuation not stated	2005 census data: 4.14 million live births and 80.8m people <20 years	Difference in treatment costs and value of lost life between current (12.3%) EBF for 6 months and the target (80%)	$12.97 billion at 90% including deaths $3.35billion excluding deaths		• Not clear how long cost data were applied for • No uncertainty accounted for
Barton et al. (2001)	USA	October 1995-Jan 1996 but all work limited to in-patient stay in NICU	A non-random sample of 60 infants (39 in BF and 41 in formula)	Difference in variable costs and net revenue between BF and FF infants at NICU	Direct variable costs: $15179 (BF) $11813 (FF) Net revenue: $46,161 (BF) $35365 (FF)	Mean difference in variable costs between BF infants and FF infants =$ 3366 (estimated) In net revenue= $10796 Note: although insignificant, FF fares better in this study	• small sample size and only NICU infants limiting generalisability • Not adequately powered to detect a difference
Buchner et al. (2008)	Netherlands	Lifetime from birth	187,910 infants born in 2005	Cost savings due to improved BF scenario compared with present situation	N/A	Savings of Euro 250 per newborn on best case scenario (100% BF ≥6months)	No uncertainty accounted for. DALY calculation is not transparent enough.

Cattaneo et al. (2006)	Italy	From birth to 1 year	A 80% powered sample of 842 newly born infants	Cost-savings by each additional months of breastfeeding	Not available	Euro 20.79 per additional month of BF (healthcare only) Euro 144.36 (healthcare + formula) Ambulatory: BF: Euro 34.69/infant CF/NBF=Euro 54.59/infant Hospital: BF: Euro 133.53/infant CF/NBF=Euro 254.03/infant	Not disease-specific. Generalisation difficult.
Drane (1997)	Australia	From birth to 1 year (health outcomes) Lifetime (special education)	Newly born infants Term=240000 Pre-term=16000	Cost-savings as difference in current and target breastfeeding rates	$11.5 million		No critical review of data used.
Hoey & Ware (1997)	USA	From birth to 12 months	A sample of 242 newly born infants out of 2140 for the HMO	Cost-savings as difference in EBF and EFF in the first6 months		$200/infant	No attempt to control for confounders although the average estimates are claimed as weighted.
Riordan (1997)	USA	Annual costs (From birth to 1 year)	Not clear. Diarrhoeal diseases= 16m episodes RSV=90,000 infants IDDM=120,000 children OM=not stated	Cost of 'not breastfeeding' as costs attributable to formula feeding	GI/diarrhoea= $291.3m OM=$660m RSV=$225m IDDM=$9.6 - $124.8m Total = $1.19-$1.30b		Estimates are crude and approximations. No justification as to whether the attributable fraction approach is correct and appropriate. No clear definition of breastfeeding provided.

Smith et al. (2002)	Australia	One year, though children 0-4 years of age included	N=1193 women in Australian Capital Territory (93% of those who agreed to participate and were retained to six months postpartum.	Artificial infant feeding attributable costs of hospitalisation for GI, AOM, respiratory illness, eczema and NEC	AUD 1.5 million at 40% breastfeeding rate and AUD 1.2 million at 60% breastfeeding rate	Not reported	• No individual level matching between breastfeeding rates and hospitalisation episodes possible • Because of this confounding in rates of hospitalisation could be a problem • Underestimation possible for GI, respiratory and eczema • Overestimation possible for NEC
Weimer (2001)	USA	From birth to 2 years Deaths (for all years)	3.9 million newly born infants in 1998; 291 LBW (for NEC)	Cost-savings achieved by EBF (at birth or 5-6 months) as opposed to present situation	Total = $3.6b (including deaths) OM=$4m GI=$5m NEC=$3b		Inclusion of indirect costs inflated COI estimates (a discussion in Bartick & Reinhold 2010)
Wight (2001)	USA	Not clear	140 very low birth weight infants	Extra costs of not using human milk		Total extra cost of not using human milk = $9669/infant Savings to NICU= $11 per $1 spent on human milk	Considers specific sub-group of individual-preterm babies who could benefit from donor milk. Resource use data derived from a single centre.

Data Table X: Papers included in full-text screening

1-37, Endnote#	Citation	Outcome of full-text review
1/1668	Altman M, Vanpee M, Cnattingius S, Norman M. Moderately preterm infants and determinants of length of hospital stay. Archives of Disease in Childhood: Fetal and Neonatal Edition 2009;94 (6):F414-F418	Exclude. • Not a cost analysis • Quantitative results on determinants of hospital length of stay
2/162	Argus BM, Dawson JA, Wong C, Morley CJ, Davis PG. Financial costs for parents with a baby in a neonatal nursery. Journal of Paediatrics & Child Health 2009;45(9):514-7.	Exclude • Private costs • Includes express/storage of breast milk in a specific population
3/113	Arnold LD. The cost-effectiveness of using banked donor milk in the neonatal intensive care unit: prevention of necrotizing enterocolitis. Journal of Human Hypertension 2002;18(2):172-177.	Exclude • CEA of an intervention
4/9	Ball TM, Wright AL. Health care costs of formula-feeding in the first year of life. Pediatrics 1999;103(4 Supplement S):870-876.	Include
5/137	Bartick M, Reinhold A. The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis. Pediatrics 2010;125(5):e1048-56.	Include
6/65	Barton AJ, Danek G, Owens B. Clinical and economic outcomes of infants receiving breast milk in the NICU. Journal of the Society of Pediatric Nurses 2001;6(1):5-10.	Include
7/3765	Battersby S, Aziz M, Bennett K, et al. The cost-effectiveness of breastfeeding peer support. British Journal of Midwifery 2004;12(4):201-205.	Exclude • CEA • No methods provided
8/6	Berridge K, Hackett AF, Abayomi J, Maxwell SM. The cost of infant feeding in Liverpool, England. Public Health Nutrition 2004;7(8):1039-1046.	Exclude • Cost of formula v. breastfeeding • Private costs only
9/623	Bonuck K, Arno PS, Memmott MM, Freeman K, Gold M, McKee D. Breast-feeding promotion interventions: good public health and economic sense. Journal of Perinatology 2002;22(1):78-81.	Exclude • No methods provided

10/4118	Buchner FL, Hoekstra J, van Rossum CTM. Health gain and economic evaluation of breastfeeding policies: Model simulation (Gezondheidswinst en kosten-batenanalyse vaninterventies op het gebied van borstvoeding : Modelberekeningen): Rijksinstituut voor Volksgezondheid en Milieu RIVM; 2008	Include
11/359	Cattaneo A, Ronfani L, Burmaz T, Quintero-Romero S, Macaluso A, Di Mario S. Infant feeding and cost of health care: a cohort study. Acta Paediatrica 2006;95(5):540-6.	Include
12/3748	Dewey KG, Heinig J, Nommsen-Rivers LA. Differences in morbidity between breast-fed and formula-fed infants. Journal of Pediatrics 1995;126(5):696-702.	Exclude • No cost analysis
13/96	Drane D. Breastfeeding and formula feeding: a preliminary economic analysis. Breastfeeding Review 1997;5(1):7-15.	Include
14/347	Floret D, Lina B, Pinchinat S, Billaud G, Ait-Belghiti F, Largeron N, et al. Epidemiology and burden of rotavirus diarrhea in day care centers in Lyon, France.[Erratum appears in Eur J Pediatr. 2008 Feb;167(2):255-6]. European Journal of Pediatrics 2006;165(12):905-6.	Exclude • No cost analysis
15/4002	Gregg P, Propper C, Washbrook E. Understanding the Relationship between Parental Income and Multiple Child Outcomes: a decomposition analysis. Bristol: Department of Economics, University of Bristol, UK, The Centre for Market and Public Organisation; 2008.	Exclude • No cost analysis
16/4034	Gregg P, Washbrook E. The Effects of Early Maternal Employment on Child Development in the UK. Bristol: Department of Economics, University of Bristol, UK, Leverhulme Centre for Market and Public Organisation; 2003.	Exclude • No cost analysis • Good ref for cognitive outcomes
17/3974	Haider S, Jacknowitz A, Schoeni R. Welfare Work Requirements and Individual Well-being: Evidence from the Effects on Breastfeeding. RAND Corporation Publications Department, Working Papers; 2002. Report No.: 02-01.	Exclude • No cost analysis • Shows negative impact of WIC on BF prevalence
18/97	Hoey C, Ware JL. Economic advantages of breast-feeding in an HMO setting: a pilot study. American Journal of Managed Care 1997;3(6):861-865.	Include

19/2852	Jegier BJ, Meier P, Engstrom JL, McBride T. The Initial Maternal Cost of Providing 100 mL of Human Milk for Very Low Birth Weight Infants in the Neonatal Intensive Care Unit. Breastfeeding Medicine 2010;5(2):71-77.	Exclude • Cost of an intervention • Good for background
20/3245	Kuzma-O'Reilly B, Duenas ML, Greecher C, Kimberlin L, Mujsce D, Miller D, et al. Evaluation, development, and implementation of potentially better practices in neonatal intensive care nutrition. Pediatrics 2003;111(4).	Exclude • No cost analysis
21/3123	McGregor J, Barseghyan M. Neurobiologically-based earning benefits of being breastfed: Longterm economic analysis. American Journal of Obstetrics and Gynecology 2005;193(6):620.	Exclude • conference abstract
22/418	Melliez H, Boelle PY, Baron S, Mouton Y, Yazdanpanah Y. [Morbidity and cost of rotavirus infections in France]. Medecine et Maladies Infectieuses 2005;35(10):492-9.	Exclude • No cost analysis
23/174	Niessen LW, ten Hove A, Hilderink H, Weber M, Mulholland K, Ezzati M. Comparative impact assessment of child pneumonia interventions. Bulletin of the World Health Organization 2009;87(6):472-80.	Exclude • CEA
24/124	Rice SJC, Craig D, McCormick F, Renfrew MJ, Williams AF. Economic evaluation of enhanced staff contact for the promotion of breastfeeding for low birth weight infants. International Journal of Technology Assessment in Health Care 2010;26(2):133-40.	Exclude • CEA • Useful, as the first economic evaluation reported from the UK
25/12	Riordan JM. The cost of not breastfeeding: a commentary. Journal of Human Hypertension 1997;13(2):93-97.	Include
26/151	Saunders JB. The economic benefits of breastfeeding. Ncsl Legisbrief 2010;18(1):1-2.	Exclude • Briefing paper • No details on methods
27/3804	Smith J. Valuing mother's milk. Aroha 2003;5(6):8-9.	Exclude • No methods provided
28/4058	Smith JP. Human Milk Supply in Australia. Food Policy 1999;24(1):71-91.	Exclude • No cost analysis

29/3655	Smith JP, Harvey PJ. Chronic disease and infant nutrition: is it significant to public health? Public Health Nutrition 2010 13 July [Epub ahead of print].	Exclude • No cost analysis
30/4049	Smith JP, Ingham LH. Breastfeeding and the Measurement of Economic Progress. Journal of Australian Political Economy 2001(47):51-72.	Exclude • No cost analysis
31/4030	Smith JP, Ingham LH. Mothers' Milk and Measures of Economic Output. Feminist Economics 2005;11(1):41-62.	Exclude • Not a cost analysis
32/7	Smith JP, Thompson JF, Ellwood DA. Hospital system costs of artificial infant feeding: estimates for the Australian Capital Territory. Australian and New Zealand Journal of Public Health 2002;26(6):543-551.	Include
33/161	Tuttle CR, Slavit WI. Establishing the business case for breastfeeding. Breastfeeding Medicine: The Official Journal of the Academy of Breastfeeding Medicine 2009;4 Suppl 1:S59-62.	Exclude • No cost analysis
34/466	Tyler M, Hellings P. Feeding method and rehospitalization in newborns less than 1 month of age. JOGNN - Journal of Obstetric, Gynecologic, & Neonatal Nursing 2005;34(1):70-9.	Exclude • No cost analysis
35/2745	Walia B. Three essays in health and labor economics: Walia, Bhavneet: Kansas State U , US; 2009.	Exclude • No cost analysis
36/3901	Weimer J. The economic benefits of breastfeeding: a review and analysis. Food Assistance and Nutrition Research Report Number 13. Washington DC: US Department of Agriculture; 2001.	Include
37/637	Wight NE. Donor human milk for preterm infants. Journal of Perinatology 2001;21(4):249-54.	Include

Appendix 6

Forty-five outcomes identified in 173 studies and reviews where evidence did not meet our criteria

The forty-five outcomes related to infant feeding examined in these 173 studies and reviews comprised 16 maternal outcomes, 3 mother and child outcomes, 25 child outcomes and 1 neonatal unit environment outcome, as follows:

Whose outcome	What outcome	Number of reviews and studies	Running total
Mother	Oesophageal adenocarcinoma	2	2
Mother	Sore nipples, engorgement	1	3
Mother	Postpartum depression	1	4
Mother	Rheumatoid arthritis	4	8
Mother	Stress response and health	1	9
Mother	Nutritional status	1	10
Mother	Body weight	1	11
Mother	Optimal health	1	12
Mother	Cardiovascular disease risk in postmenopausal women	1	13
Mother	Thyroid cancer	1	14
Mother	Postpartum blood pressure	1	15
Mother	Postpartum psychiatric morbidity	1	16
Mother	Postpartum ovulation	1	17
Mother	Hospitalisation for gallbladder disease	1	18
Mother	Pancreatic cancer	1	19
Mother	Return of menstruation	1	20
Mother and child	Bone outcomes	10	30
Mother and child	Communication	1	31
Mother and child	Maternal concerns about stool hardness	1	32
Child	Eczema and atopic dermatitis	12	44
Child	Dental caries	7	51
Child	Allergy	21	72
Child	Wheeze	8	80
Child	Weight	12	92
Child	Growth	20	112
Child	Inflammatory bowel disease (IBD)	5	117
Child	Mother-to-infant transmission of hepatitis C virus infection	1	118

Child	Infantile hypertrophic pyloric stenosis	2	120
Child	Nutrition	6	126
Child	Other cancer (not leukaemia)	6	132
Child	Psychiatric diagnoses in later life	3	135
Child	Crying/ colic	4	139
Child	Sleep	1	140
Child	Urinary tract infection	1	141
Child	Lung function later life	3	144
Child	Menopause	2	146
Child	Development	3	149
Child	HIV	10	159
Child	Procedural pain	5	164
Child	Immunity-related conditions	4	168
Child	Health and survival	1	169
Child	Measles	1	170
Child	Determinants of insulin secretion and sensitivity at age 50	1	171
Child	Nappy rash	1	172
Neonatal unit environment	Pathogens in feeding tubes	1	173

Appendix 7

Biological mechanisms related to the eight shortlisted outcomes

To assess plausibility as part of our final decision on the outcomes to be examined in our economic analyses, we examined the likely mechanisms that would explain the association between outcomes and infant feeding. These are summarised here.

How is gastrointestinal infection in infants related to infant feeding?

Gastrointestinal infection is common in childhood and globally is a leading cause of post-neonatal infant mortality. It results in diarrhoea and vomiting, which lead rapidly to dehydration and electrolyte imbalance in young infants (Lissauer and Clayden, 2012). The exposure to risks differs between those who are not breastfed at all, and those who are not exclusively breastfed and it will also relate to the environment in which the family lives (Chien and Howie, 2001); for a good summary see (Lawrence and Lawrence, 2005). Several mechanisms may explain the increased risk of gastrointestinal infection in infants who are not breastfed. Breastmilk provides specific humoral and cellular immunity that protects the infant from pathogens to which the mother is exposed, maximising the protection against infection and tailoring it to the circumstances each child will encounter (Hamosh, 2001, Nathavitharana et al, 1994). A range of other immune factors also present in breastmilk such as oligosaccharides, glycoproteins, and lactoferrin provide additional non-specific protection against infection and encourage a healthy gut flora (Hamosh, 1998, Hanson, 2004). Breastmilk substitutes do not provide either specific or non-specific immune protection.

A further risk to the infant is related to the formula itself, which can be contaminated during manufacture, transport, storage and use (e.g. (Baker, 2002)). Bottles and teats can also be contaminated and act as a further potential source of infection (European Food Safety Authority (EFSA) Scientific Panel on Biological Hazards, 2004, Renfrew et al, 2008).

How is respiratory tract infection in infants related to infant feeding?

It has been known for many years that not being breastfed is associated with an increased rate of respiratory infection (e.g. (Downham et al, 1976). Breastfeeding confers non-specific and specific immune protection upon the mucosal lining of the upper and lower respiratory tract through mechanisms similar to those operating in the gut (Hanson, 2004, Hanson LA, 2009, Ogra, 2009); see above.

How is acute otitis media related to infant feeding?

See above in regard to respiratory tract infection; the middle ear is in continuity with the upper respiratory tract (through the Eustachian tube) and thus is protected in the same way.

How is necrotising enterocolitis related to infant feeding?

Necrotising enterocolitis (NEC) is an inflammatory condition of the newborn gut, the pathology of which is incompletely understood. The incidence of NEC is inversely proportional to birthweight and gestation and is further increased in the presence of co-morbidities such as lung disease and persistent ductus arteriosus. There is an association with blood transfusion and enteral feeding but NEC can occur even in babies exclusively parenterally fed. Administration of corticosteroids pre- or postnatally is associated with a reduction in risk. The mortality associated with NEC is high (between 15-30%) and it remains a leading cause of late neonatal mortality among the very low birthweight population. About 25% of affected infants will require laparotomy and resection of affected gut, many of whom are subsequently affected by intestinal failure of varying duration (Lin and Stoll, 2006, Lin et al, 2008).

It has been postulated that the association between NEC and enteral feeding is explained by a triad of factors: 1) abnormal gut microbial colonisation leading to presence of pathogens, 2) impairment of gut perfusion secondary to circulatory disturbance in a sick baby, 3) presence of undigested nutrients (particularly milk protein) in the gut lumen as a consequence of immature gut motility and absorption in the preterm baby. This has been termed the 'Santulli hypothesis' (Kosloske, 1984). If this explanation is accepted human milk could reduce the risk of NEC in the following ways: 1) through its effect on promoting colonisation of the gut lumen by bifidobacteria, 2) by preventing mucosal adherence of pathogens through the action of secretory immunoglobulin A and 3) through reducing the luminal content of undigested nutrients, the digestibility of breastmilk nutritional proteins being particularly high. In relation to the fist possibility there is evidence that administration of cultured bifidobacteria reduces the risk of NEC (AlFaleh K et al, 2008) and there are currently randomised trials in progress testing this possibility.

Current interest is also focused on the unique anti-inflammatory properties of human milk. Immature intestinal cells appear to show enhanced propensity to secrete interleukin-8 (IL-8) in response to stimuli such as the presence of microbe associated molecular patterns. This may be the result of increased expression of toll-like receptors in the immature intestine (Nanthakumar et al, 2011). It has been shown in vitro that human milk components decrease this release of IL-8 suggesting that human milk is able to suppress the innate inflammatory response which appears to underlie NEC (Nanthakumar et al, 2011, Claud et al, 2003).

How is breast cancer in mothers related to infant feeding?

Breast cancer is the most common cancer occurring in the UK (Office for National Statistics, 2010), and the third most common cause of cancer death. Not breastfeeding is one of several reproductive factors related to an increased risk of developing breast cancer; women without children, or who have an early menarche (start of menstrual cycles) or late menopause also have an increased risk (Colditz and Rosner, 2006). These factors suggest that hormonal mechanisms involving oestrogen and progesterone act on the development of breast cancer. Some suggest the possibility that the number of menstrual cycles a woman experiences may be important (Lord et al, 2008), and breastfeeding reduces the

number of menstrual cycles a woman experiences, thereby reducing her lifetime exposure to oestrogen. It has also been hypothesised that breastfeeding may act on breast cancer risk through different mechanisms to these other reproductive factors (Ma et al, 2006).

How are cognitive outcomes related to infant feeding?

The socio-cultural patterning of infant feeding in Western industrialised societies may result in confounding by socio-economic status, and the parents' IQ and educational attainment. There are additional plausible mechanisms which directly or indirectly could explain differences in cognitive and behavioural outcomes related to the method of feeding. Breastmilk contains a range of nutrients and other factors that directly impact on growth and on physical and neurological development at a critical period in brain and nervous system development (Michaelsen et al, 2009). Infants who are not breastfed experience increased risk of infectious diseases, which may adversely affect their childhood development (see e.g. sections on gastrointestinal, respiratory and ear infection). Increased maternal touch has also been shown to be related both to improved cognitive outcomes and to breastfeeding (Feldman and Eidelman, 2003).

How is Sudden Infant Death Syndrome related to infant feeding?

Not being breastfed could increase in Sudden Infant Death Syndrome (SIDS) for many reasons (Mitchell 2004). The host of immune factors in breastmilk described in previous sections in relation to gastrointestinal infection, respiratory and ear infections (e.g. (Howie, 2002) actively protect the infant from viral infections that could contribute to the underlying cause of SIDS. Breastfed infants also have more arousals during sleep than those who are formula fed; this has been shown to be most marked at 2-3 months of age, coinciding with the peak incidence of SIDS (Horne et al, 2004). The sleeping behaviour of breastfeeding dyads also differs from that of non-breastfeeding mothers and infants; breastfeeding women appear to be more responsive to the movement of their infants, for example (Ball et al, 2012).

How is early years obesity related to infant feeding?

A range of mechanisms could explain the observed association between not being breastfed and the development of overweight and obesity (Arenz et al, 2004, Ozanne, 2009). There are inherent differences in the content of breastmilk and formula; moreover the composition of breastmilk changes during a feed in such a way that the infant can regulate energy intake (Woolridge et al, 1990). The pattern of growth and tissue deposition in infancy differs between breast and formula fed infants (Gale et al, 2012). The metabolic response to feeding formula and breastmilk differs, particularly with regard to insulin secretion (Lucas et al, 1980). Formula contains more protein per unit volume than breastmilk (Heinig et al, 1993), and breastmilk contains leptin, which has been shown in animal models to have a role in appetite regulation (Gruszfeld D, 2005); these differences may result in programmed changes in appetite. It is also possible that behavioural aspects in both infants and mothers may play a part in the development of obesity; it is easier for breastfed infants to moderate their own intake by coming off the breast (Stuart-Macadam

and Dettwyler, 1995) whereas carers of bottle fed infants can continue to feed after the infant has had enough (Taveras et al, 2004).

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Appendix 8

Population attributable and preventive fractions

We originally planned to estimate population attributable fraction (PAF) to estimate the proportion of cases that were attributable to 'not breastfeeding'. However, this proved to be difficult because the standard formulae for PAF (Bruzzi et al 1985) are for exposures which result in an increased risk of disease (e.g. smoking) rather than a protective effect. For example:

$$PAF = P_{E/D} (RR-1) / RR$$

where RR=risk ratio and $P_{E/D}$ is the proportion of the population exposed among the cases (here this is the prevalence of BF in those who have the disease).

Using these formulae for a RR which is less than 1 results in a negative PAF which is meaningless. It is possible to address this problem using reverse coding and inverting the results (e.g. using the RR for 'not breastfeeding' which is greater than 1, and calculating the PAF for 'not breastfeeding'). However, this approach only works for a binary exposure (e.g. breastfed versus not breastfed) rather than an exposure which has several categories (e.g. breastfeeding duration).

An alternative approach which allowed us to incorporate an exposure which had several categories and a 'protective effect' (risk ratios less than 1) was to use the preventive fraction (PF). For example [Equation 10 in Benichou 2001]:

$$PF = P_E (1-RR)$$

where RR is the risk ratio (which is less than 1) and P_E = the proportion of the population exposed (i.e. the prevalence of BF in the population).

Note that there is a different interpretation for the PAF using reverse coding and the PF:

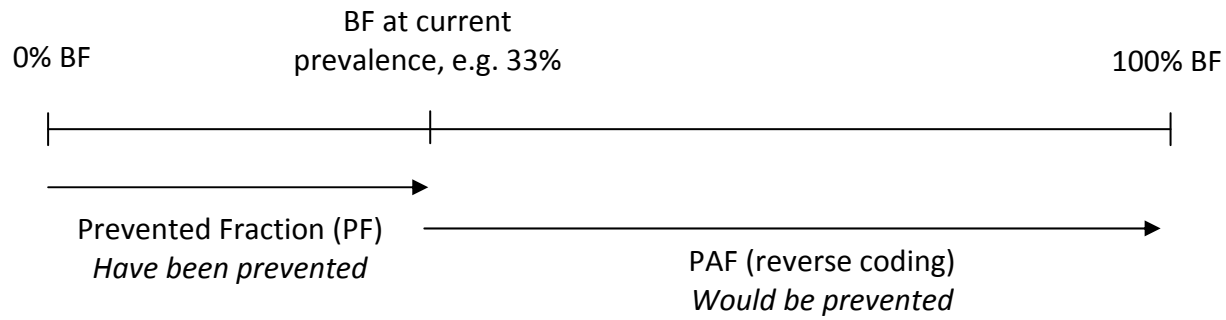
The different interpretation of the results from the PAF for 'not breastfeeding') and the PF for breastfeeding is subtle but important. They use different denominators and this is illustrated in Figure 8.1 below.

- The PAF using reverse coding is the PAF for not breastfeeding and shows the percentage of cases could be prevented if all formula-fed babies were breastfed.

- The PF for breastfeeding shows the percentage of cases which were prevented by the current level of breastfeeding.

Where possible, we have included estimates of the PAF and/or PF as appropriate. These are presented merely to give a rough estimate of the population impact of the breastfeeding, but these results have not been included in the economic models.

Figure 8.1: Figure showing different interpretation of the PF for breastfeeding and the PAF for not breastfeeding



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Appendix 9

Review of evidence to inform model parameters: sources and evidence summary tables

Sources

The primary aim of this search was to locate papers/sources that provide data on incidence of gastroenteritis, respiratory illnesses, otitis media and necrotising enterocolitis in children and breast cancer in women; costs of treating an episode of those health outcomes; and/or hospitalisation and primary care use specific to the above mentioned health outcomes. The estimates must refer to the United Kingdom as a whole or one of the four countries in the UK.

The following databases/sources were searched:

- Centre for Reviews and Dissemination (CRD) which includes Cochrane, HTA and NHS Economic Evaluation Database
- NICE guidance
- PubMed
- Websites (Joint Committee on Vaccination and Immunisation; Cancer Research UK; Neonatal Networks; Office for National Statistics; The Information Centre)
- Snowballing (locating from other papers)

The first database was expected to pick up randomised control trials and economic evaluations while other databases/websites were expected to pick up cross-sectional and cohort studies, including cost-of-illness, and other relevant reports.

It is important to note that due to resource constraints, the search for the parameters was limited to the above databases/sources which the researchers' experience suggests are likely to be the most likely sources of relevant literature

Reviewed sources for parameters in infantile gastroenteritis model

Input parameter	Source	Description from the source (summarised if necessary)	Comments	Extent of relevance to our work
Birth and death rates	ONS 2009	The total UK population is 61792000 in 2009 and ONS estimates that the live birth rate is 12.8/1000. This means the total number of live birth in 2009 in the UK is 790,938 (61792000*12.8/1000). 2009 infant mortality = 4.6 per 1000 live births. 2009 neonatal mortality rate per 1000 live births=3.1.	These are the most recent data on birth and deaths available from the Office for National Statistics and regarded as the most relevant.	Relevant as the reference population in this study is all infants born in the UK
Breastfeeding rates	Infant Feeding Survey 2005	A completely unclustered sample of 19,848 births was selected from all births registered in the period August to October 2005 in the United Kingdom. Samples were designed to be representative of all births during that period. Three stages of data collection were conducted: Stage 1: infants 4-10 weeks old; Stage 2; infants 4-6 months old; Stage 3: infants 8-10 months old. A total 9,416 mothers completed and returned all three questionnaires. Mothers were only contacted in later Stages of the survey if they had responded to the previous Stage, and so the effect of non-response at each Stage was cumulative. 47% of all mothers who were initially sampled responded to all three Stages of the surveys, and this ranged from 50% in both Scotland and Northern Ireland to 46% in England. Analysis of the 2005 survey showed a consistently lower response rate in all countries among younger mothers and in areas of higher deprivation at all Stages of the survey. However, all data were weighted to correct for differential sampling and for differential response rates among different groups. Prevalences of exclusive and partial breastfeeding are provided.	Despite limitations, this remains the most widely used source for breastfeeding prevalence in the UK. There are various country-specific surveys (for all 4 UK countries) that capture infant feeding, they differ in the design, definitions and sample size. IFS provides the same methodology for all 4 countries.	IFS is particularly relevant to current study for its two strengths: (a) Data are collected at various stages until the child reaches approximately 9 months old; (b) It collects long term comparable data for all UK countries.

		For the UK, the following is estimated: Exclusive breastfeeding at birth 65%; at 1 week 45%, 6 weeks 21%, 4 months 7% and 6 months <0.5%.		
Odds ratio in favour of breastfeeding on gastrointestinal infections GI	WP 1 (Renfrew et al.) and WP 2 (Quigley) of the current project	The two studies that are relevant are Quigley et al. (2006), a case-control study; and Quigley et al. (2007), Millennium Cohort Study (MCS). Quigley et al. (2006) results show the "current" effect of breastfeeding on GI infection i.e. if you are currently breastfed, how does this reduce your risk of GI infection. The data is from 1993-96. It does not estimate the prolonged effect of breastfeeding i.e. if you are breastfed until age 3 months, how does this reduce your effect of GI infection when you are 6 months old, for example. The outcome is GP cases of GI infection. The OR for breast milk only is 0.26 (CI: 0.10-0.64) and OR for breast & formula is 0.60 (CI-not given), compared to formula (OR=1). Note that "breast milk only" means either "EBF" or "breast milk & solids" and all ORs adjusted for age, sex, weaning, social class, travel, use of a food mixer, and contact with person in household & outside household. The results from the second study (Quigley et al. 2007) show the "current" effect of breastfeeding on GI infection. The outcome is hospitalisation for GI infection and the data is for infants under 8 months in 2000-2002. The OR for partial breastfeeding is 0.63 (CI-0.32-1.25) and for exclusive breastfeeding is 0.37 (CI- 0.18-0.78), compared to formula (OR=1). The odds ratios are adjusted for month (i.e. baby's age), mother's age at delivery, mode of delivery, and mother's education. Other studies considered in WP2 for GI outcome are Howie et al. (1990); Fisk et al. (2011) and Baker et al. (1998).	These OR are based on systematic reviews and synthesis undertaken as part of the current project (WP1 and WP2). This is based on the best available data reported from UK as well as industrialised countries similar to the UK.	Relevant.

Incidence of GI	Van Damme et al. (2007) JID article	A prospective, multicenter, observational study was conducted during the 2004–2005 season in selected areas of Belgium, France, Germany, Italy, Spain, Sweden, and the United Kingdom, to estimate the incidence of acute gastroenteritis (AGE) and rotavirus gastroenteritis (RVGE) in children <5 years of age seeking medical care in primary care, emergency department, and hospital settings. AGE was defined as an episode of at least 3 loose stools, at least 3 watery stools, or forceful vomiting associated with gastroenteritis occurring during a 24-h period in the 7 days before the medical visit; the episode must have been preceded by a symptom-free period of 14 days. A total of 2846 children with AGE were included in the study, and, of the 2712 children for whom ELISA results were available. For the UK, the estimated annual incidence of AGE for 1-5 months was 9.88 per 100 children and for 6-11 months 12.34 per 100 children.	Sample size was calculated in advance to power the study (precision 0.01 and 95% CI). The UK sample came from Wirral Peninsula. This study also provides data on incidences by care (primary or hospital) in addition to overall incidence. Children presenting >1 during study period were considered to be separate cases. This is the only study we have found that provides *overall* incidence of GI in infants. Note there are a few studies out there reporting *partial* incidences such as that of hospitalisation for rotavirus (e.g. Riordan and Quigley 2004; Ryan et al. 1996).	This is the average of estimates available for 1-5 months and 6-11 months old. The UK sample is from Wirral Peninsular. The study selected from each country a study area that is middle-size (a town/city of 100k-250k inhabitants and surrounding rural population of ~100k). All hospitals and A&E departments that might see children with gastroenteritis were included plus a convenience sample of GPs within the catchment area. The rates reported include estimation for the entire population based on this sample, applied consistently across all countries. The London Health Observatory (LHO) data suggests that this area has a population of 308k (2010) and infant mortality rate of 4.68 (not significantly different from England average 4.71). Other indicators differ from England. In the absence of other data on GI specific overall incidence rate in infants, this data is used with caveat.

Care episode incidences	DH (2011); Quigley et al. (2007); Tam et al. (2011), Harris et al. (2007), Martin et al. (2009), Lorgelly et al. (2008), ONS (2011), Whitburn et al. (2011)	There are three sources which provide care incidence data. The most recent one is from the Department of Health based on hospital episode statistics and refers to incidence of hospitalisation in infants (17.2 hospitalisations per 1000 live births in England). Similar statistics are reported from Quigley et al. 2007 (16 hospital admissions per 1000 infants in England). However, our search did not reveal any directly relevant data on primary care. Based n GPRD dataset for 2002-03, Harris et al. (2007) estimate that the annual incidence of GP consultations for rotavirus infection in children <5 years is 44.3 (39.4-49.3) per 1000 children. They estimate that this constitutes 25% of all GI infections. Martin et al. (2009) update this figure as 31%. Putting these figures together, if we assume that 25-31% of total GP consultations for GI are for rotavirus, the annual incidence of GP consultations for GI is between 142-177 per 1000 children. A recent study (Tam et al. 2011) based on community (n=6836) and GP presentation (n=1254) samples suggests that this rate could have been between 85 and133 per 1000 person years in 2008-09. They had larger uncertainties (60-220). As our reference window is one year after applying all-cause mortality, this unit could be approximated as "per 1000 children" in our case. Based on a very small sample (n=136), Lorgelly et al. (2008) estimated that the mean number of GP consultations for GI is 1.81 per episode of GI. If we apply this to our reference population of 788,486 and use van Damme et. al. (2007) incidence data of 11.1 per 100 children, the incidence would be 201 per 1000 children. Based on QRESEARCH data, the Office for National Statistics suggests the overall GI consultation rates in primary care in <5 years is 3.03 per person in 2009 and	The DH (2001) estimates based on HES data are the most obvious source and so is the RCGP data for primary care. The RCGP data is the most up-to-date, is based on 105 practices across England (regional health authority representation of 0.66% in East of England to 2.56% in London) although it is based on weekly reports and therefore is not free from double counting if two different Read codes are entered within the same week. The extent of this bias is now known.	Hospital admissions are relevant and to be presented as the most robust costs estimate. The GP data to be treated with caution.

		62.1% of which are with the GP. A more recent study (Whitburn et al. 2011) based on a sample of parental reports of presenting symptoms (n=2491) suggests that in 2005-07, for every 100 GP consultations, 13 were for GI. This means the annual GP consultation rate for GI in <5 year olds is 244 per 1000 children. Therefore, the conservative estimate for GP consultation rates in children under 5 (the closest age group relevant to our reference population) is about 200 (85-244) per 1000 children. The most recent data for primary care came from Royal College of GPs Annual Report for 2010. According to this report, the incidence of primary care consultations for RTI clinical diagnosis is 37502.02523 per 100,000 infants (<1 year old).		

Unit costs of a gastroenteritis episode	Lorgelly et al. (2008). Epidemiology. Infect. 136, 34-43	Total cost of illness per episode of gastroenteritis in 2001/2002 prices were: £59.91 with SD 125.67 and range 19-1187 to health care sector. This is based on a cohort of 136 children. The study consisted of twenty GPs in East Anglia, over three rotavirus seasons (the winter months between December 2000 and April 2003), collecting faecal specimens from children aged <5 years who presented with symptoms of gastroenteritis, where gastroenteritis was defined as the presence of vomiting and/or diarrhoea. Parents or carers of these children were asked to complete a questionnaire (available from authors on request) detailing severity of illness, health-care resource use, personal medical expenditure, changes in child-care patterns and associated costs, time off work and lost income due to their child illness.	This is a community-based study on a small sample. However, the study has collected detailed information on health resource use such as number of GP visits, nurse visits, prescriptions, hospital attendances and days in hospital for the entire cohort. They have attempted to include ALL costs to NHS including NHS Direct. Not included are the costs of lab tests as it was not universal practice to test stool samples from the community. Their unit costs data come from a widely referred source (PSSRU and BNF).	Relevant as we recognise most of the GI costs are going to fall in the community, i.e. primary care and the study results reflect that [GP surgery visits alone costs on average £31.34 compared to hospital stays (£12.98) per GI episode]. Sensitivity analysis can help establish the level of uncertainty around estimates using the variation around the input parameters presented in this paper. The study covered three rotavirus seasons, giving a good coverage of GI. The child mortality in East Anglia (from where the sample came in) is similar to that of England (4.20 compared to 4.70) as are the breastfeeding initiation rates (76.2 compared to 75.1) - ER PHO data (http://fingertips.erpho.org.uk/childhealth).

Unit cost of primary care consultation	Curtis (2010)	This is the most widely used and robust source for unit cost in health and social care. Per surgery consultation lasting 11.7 minutes is estimated at £36 with qualifications costs (£32 without it) and includes direct care staff costs. The estimation builds on assumptions like remuneration, qualification costs, ongoing training, capital costs, overhead, travel and working time. The per-surgery consultation minutes are based on "The Information Centre (2007) 2006/07 UK General Practice Workload Survey, Primary Care Statistics, The Information Centre, Leeds." This book also provides different estimates based on where the GP consultation took place, e.g. surgery (£36), clinic (£53), telephone (£22), and home visit (£122). For the current analysis, the cost of surgery-consultation is used as conservative estimate. All prices are 2009-10.	Most obvious source of data for GP unit costs.	Relevant.
Unit cost of hospitalisation for GI	Department of Health, NHS Reference Costs 2009-10	The unit cost of a hospital admission is based on the NHS Reference Costs and is derived as follows: Step 1: Identify ICD-10 codes for GI based on Department of Health (2011) Step 2: Using ICD-10 to HRG3.5 online explorer (http://www.ic.nhs.uk/services/the-casemix-service/using-this-service/reference/archived-past-hrg-v35-grouper-information/on-line-hrg-v35-explorer), identify corresponding HRG3.5 titles Step 3: Match these titles in HRG4 to identify corresponding HRG4 codes in 2009-10 NHS Reference Costs Step 4: Obtain activity weighted average costs to reflect the hospital admission unit cost.	Most obvious source of data for hospital admissions costs	Relevant.

Reviewed sources for parameters in infantile respiratory illness model

Input parameter	Source	Description from the source (summarised if necessary)	Comments	Extent of relevance to our work
Birth and death rates	ONS 2009	The total UK population is 61792000 in 2009 and ONS estimates that the live birth rate is 12.8/1000. This means the total number of live birth in 2009 in the UK is 790,938 (61792000*12.8/1000). 2009 infant mortality = 4.6 per 1000 live births. 2009 neonatal mortality rate per 1000 live births=3.1.	These are the most recent data on birth and deaths available from the Office for National Statistics and regarded as the most relevant.	Relevant as the reference population in this study is all infants born in the UK
Breastfeeding rates	Infant Feeding Survey 2005	A completely unclustered sample of 19,848 births was selected from all births registered in the period August to October 2005 in the United Kingdom. Samples were designed to be representative of all births during that period. Three stages of data collection were conducted: Stage 1: infants 4-10 weeks old; Stage 2; infants 4-6 months old; Stage 3: infants 8-10 months old. A total 9,416 mothers completed and returned all three questionnaires. Mothers were only contacted in later Stages of the survey if they had responded to the previous one, and so the effect of non-response at each Stage was cumulative. 47% of all mothers who were initially sampled responded to all three Stages of the surveys, and this ranged from 50% in both Scotland and Northern Ireland to 46% in England. Analysis of the 2005 survey showed a consistently lower response rate in all countries among younger mothers and in areas of higher deprivation at all Stages of the survey. However, all data were weighted to correct for differential sampling and for differential response rates among different groups. Prevalences of exclusive and partial breastfeeding are provided. For the UK, the following is estimated: Exclusive breastfeeding at birth 65%; at 1 week 45%, 6 weeks 21%, 4 months 7% and 6 months <0.5%.	Despite limitations, this remains to be the most widely used source for breastfeeding prevalence in the UK. There are various country-specific (for all 4 countries) surveys that capture infant feeding, they differ in the design, definitions and sample size. IFS provides the same methodology for all 4 countries.	IFS is particularly relevant to current study for its two strengths: (a) Data are collected at various stages until the child reaches approximately 9 months old; (b) It collects long term comparable data for all UK countries.

Odds ratio in favour of breastfeeding on LRTI	WP 1 (Renfrew et al.) and WP 2 (Quigley) of the current project	The studies that are relevant are Howie et al. (1990); Wilson et al. (1998), both from Dundee Cohort Study, Quigley et al. (2007) from Millennium Cohort study, and Fisk et al. (2011), Southampton Women's Study. Further analysis done by MQ on Millennium Cohort show the "current" effect of breastfeeding on LRTI hospitalisations for infants under 8 months in 2000-2002. The OR for exclusive breastfeeding is estimated at 0.70 (CI- 0.49-0.98). The OR for any breastfeeding is 0.67 (CI-0.52-0.88). The odds ratios are adjusted for month (i.e. baby's age), mother's age at delivery, mode of delivery, household income, whether the baby was the first born, mother's current smoking status, and family history of asthma. These estimates are comparable with other studies and lie between 0.65 and 0.70.	These OR are based on systematic reviews and synthesis undertaken as part of the current project (WP1 and WP2). This is based on the best available data reported from UK as well as industrialised countries similar to the UK.	Relevant as these data reflect the policy scenario we are working on.
Incidence of hospitalisation for LRTI	DH (2011)	The most recent data are from the Department of Health based on the hospital episode statistics in England and refers to incidence of hospitalisation in infants (59.1 hospital admissions per 1000 live births in 2009/10). Similar statistics is reported from Quigley et al. 2007 (48 hospital admissions per 1000 infants). The DH data is based on 41 different diagnoses based on J-chapter of the ICD-10.	These are the actual numbers of hospital admissions recorded in England and no other estimates based on study sample are deemed more accurate than this.	Relevant as it is the most obvious source of data for hospital admission incidences.

Incidence of primary care for LRTI	Gulliford et al. (2009); Ashworth (2004); Whitburn et al. (2011); Hansell et al. (1999); Deshpande and Northern (2003); NICE (2008); RCGP (2010)	A number of studies provide some estimates of consultation rates in primary care and/or use of antibiotics following such consultations. The most relevant is Gulliford et al. (2009) who provide most recent estimates (for 2006) based on UK General Practice Research Database (GPRD).The GPRD covers ~5% of the populations of England and Wales and holds data on diagnoses and prescribing from 1987 onwards. Gulliford et al. included 78 practices. From the population of all registered subjects, a sample was compiled by taking an independent random sample of 10,000 subjects for each year of study. Subjects were sampled with replacement and 94,470 subjects provided 100,000 person years of study. Age- and sex-specific consultation rates were estimated and these were used to calculate age-standardised rates. The paper provides figures separately for "Acute bronchitis, chest infection and pneumonia" which broadly resembles definitions used by the DH (2011) for hospitalisation incidence data and Quigley et al. (2007) on odds ratios. The age-standardised consultation rates for "acute bronchitis, chest infection and pneumonia" in 2006 were: 61.0 per 1000 patients per year (female); 44.9 (male) and proportions of consultations with antibiotics prescribed were: 86.4% (female) and 89.1% (male). This paper suggests that consultation rates decreased over time (the earliest reported year is 1997 when the rates were 78.4 for males and 59.8 for females). If we assume a similar trend, the rates in 1992 would be higher and comparable to Hansell et al. (1999) study which suggests in 1992 the rates were 79.6 (combined). The source of data is the same, i.e. GPRD, although the derivations of consultation rates differ - age-standardised in Gulliford et al. and 0-4 years in Hansell et al. Other studies present data for overall population (not age-standardised as we need) and also cover only a part of respiratory illness, e.g. respiratory syncytial virus disease as in Deshpande and Northern (2003). The most recent data came from Royal College of GPs Annual Report for 2010. According to this report, the incidence of primary care consultations for RTI clinical diagnosis is 312,545.5024 per 100,000 infants (<1 year old).	The UK GPRD is considered a large dataset covering primary care diagnosis and consultations in the UK. A study by Hansell et al. (1999) compared the findings from GPRD with the 4th Morbidity Survey in General Practice (MSGP4) and found that "GPRD appears to be valid for primary care epidemiological studies by comparison with MSGP4 and offers advantages in terms of large size, a longer time period covered, and ability to link prescriptions with diagnosis". There have been some issues around missing data and miscoding of diagnoses. Nevertheless, GPRD remains the best source for primary care data in the UK. The RCGP data is the most up-to-date, is based on 105 practices across England (regional health authority representation of 0.66% in East of England to 2.56% in London) although it is based on weekly reports and therefore is not free from double counting if two different Read codes are entered within the same week. The extent of this bias is now known.	RCGP data is the most obvious one to use. However, other data needs to be used in sensitivity analysis.

Unit cost of primary care consultation	Curtis (2010)	This is the most widely used and robust source for unit cost in health and social care. Per surgery consultation lasting 11.7 minutes is estimated at £36 with qualifications costs (£32 without it) and includes direct care staff costs. The estimation builds on assumptions like remuneration, qualification costs, ongoing training, capital costs, overhead, travel and working time. The per-surgery consultation minutes are based on "The Information Centre (2007) 2006/07 UK General Practice Workload Survey, Primary Care Statistics, The Information Centre, Leeds." This book also provides different estimates based on where the GP consultation took place, e.g. surgery (£36), clinic (£53), telephone (£22), and home visit (£122). For the current analysis, the cost of surgery-consultation is used as conservative estimate. All prices are 2009-10.	Most obvious source of data for GP unit costs.	Relevant.
Unit cost of hospitalisation	Department of Health, NHS Reference Costs 2009-10	The unit cost of a hospital admission is based on the NHS Reference Costs and is derived as follows: Step 1: Identify ICD-10 codes for LRTI based on Department of Health (2011) Step 2: Using ICD-10 to HRG3.5 online explorer (http://www.ic.nhs.uk/services/the-casemix-service/using-this-service/reference/archived-past-hrg-v35-grouper-information/on-line-hrg-v35-explorer), identify corresponding HRG3.5 titles Step 3: Match these titles in HRG4 to identify corresponding HRG4 codes in 2009-10 NHS Reference Costs Step 4: Obtain activity weighted average costs to reflect the hospital admission unit cost.	Most obvious source of data for hospital admissions costs	Relevant.

Unit cost of antibiotics	NICE (2008)	The NICE guidance on RTI- antibiotic prescribing provides some useful data on antibiotics. Table 4 (p. 15) lists the course cost of antibiotics for different diagnoses and includes both adults and children. For this study, the figure corresponding to "Acute cough/acute bronchitis" has been taken as this is the closest category for LRTI. The course cost is estimated at £1.61 in 2008-09 prices. These figures are based on a number of assumptions: (a) the typical drugs assumed to treat RTI (note, this also includes LRTI) are amoxicillin, clarithromycin, phenopythylpenicillin and erythromycin; (b) 22% of those who receive a primary care consultations are children under 18; (b) the prices come from the PPA NHS electronic Drug Tariff.	The actual unit costs may differ if the same process is repeated for children under 1 year of age. However, this would require a re-analysis based on several parameters and is not feasible under this project. Given small amount (£1.61), the use of current figure will not have a significant impact on the total cost-savings to be estimated in this project.	Relevant with caveat

Reviewed sources for parameters in infantile acute otitis media model

Input parameter	Source	Description from the source (summarised if necessary)	Comments	Extent of relevance to our work
Birth and death rates	ONS 2009	The total UK population is 61792000 in 2009 and ONS estimates that the live birth rate is 12.8/1000. This means the total number of live birth in 2009 in the UK is 790,938 (61792000*12.8/1000). 2009 infant mortality = 4.6 per 1000 live births. 2009 neonatal mortality rate per 1000 live births=3.1.	These are the most recent data on birth and deaths available from the Office for National Statistics and regarded as the most relevant.	Relevant as the reference population in this study is all infants born in the UK
Breastfeeding rates	Infant Feeding Survey 2005	A completely unclustered sample of 19,848 births was selected from all births registered in the period August to October 2005 in the United Kingdom. Samples were designed to be representative of all births during that period. Three stages of data collection were conducted: Stage 1: infants 4-10 weeks old; Stage 2; infants 4-6 months old; Stage 3: infants 8-10 months old. A total 9,416 mothers completed and returned all three questionnaires. Mothers were only contacted in later Stages of the survey if they had responded to the previous one, and so the effect of non-response at each Stage was cumulative. 47% of all mothers who were initially sampled responded to all three Stages of the surveys, and this ranged from 50% in both Scotland and Northern Ireland to 46% in England. Analysis of the 2005 survey showed a consistently lower response rate in all countries among younger mothers and in areas of higher deprivation at all Stages of the survey. However, all data were weighted to correct for differential sampling and for differential response rates among different groups. Prevalences of exclusive and partial breastfeeding are provided. For the UK, the following is estimated: Exclusive breastfeeding at birth 65%; at 1 week 45%, 6 weeks 21%, 4 months 7% and 6 months <0.5%.	Despite limitations, this remains to be the most widely used source for breastfeeding prevalence in the UK. There are various country-specific (for all 4 countries) surveys that capture infant feeding, they differ in the design, definitions and sample size. IFS provides the same methodology for all 4 countries.	IFS is particularly relevant to current study for its two strengths: (a) it collects data at various stages until the child reaches approximately 9 months old; (b) it collects long term comparable data for all UK countries.

Odds ratio in favour of breastfeeding on AOM	WP 1 (Renfrew et al.) and WP 2 (Quigley) of the current project	The studies that are relevant are Howie et al. (1990); Wilson et al. (1998), both from Dundee Cohort Study, Quigley et al. (2007) from Millennium Cohort study, and Fisk et al. (2011), Southampton Women's Study. Further analysis done by MQ on Millennium Cohort show the "current" effect of breastfeeding on LRTI hospitalisations for infants under 8 months in 2000-2002. The OR for exclusive breastfeeding is estimated at 0.70 (CI- 0.49-0.98). The OR for any breastfeeding is 0.67 (CI-0.52-0.88). The odds ratios are adjusted for month (i.e. baby's age), mother's age at delivery, mode of delivery, household income, whether the baby was the first born, mother's current smoking status, and family history of asthma. These estimates are comparable with other studies and lie between 0.65 and 0.70.	These OR are based on systematic reviews and synthesis undertaken as part of the current project (WP1 and WP2). This is based on the best available data reported from UK as well as industrialised countries similar to the UK.	Relevant as these data reflect the policy scenario we are working on.

Incidence of primary care for AOM	Gulliford et al. (2009); Ashworth et al. (2004) NICE (2008); Hansell et al. (1999); Whitburn et al. (2011); RCGP (2011)	This paper is by Gulliford et al. (2009) who provide most recent estimates (for 2006) based on UK General Practice Research Database (GPRD).The GPRD covers ~5% of the populations of England and Wales and holds data on diagnoses and prescribing from 1987 onwards. The study by Gulliford et al. included 78 practices. From the population of all registered subjects, a sample was compiled by taking an independent random sample of 10,000 subjects for each year of study. Subjects were sampled with replacement and 94,470 subjects provided 100,000 person years of study. Age- and sex-specific consultation rates were estimated and these were used to calculate -age-standardised rates. The paper provides figures separately for "otitis media and earache" which broadly resembles with the definitions used by DH (2011) for hospitalisation incidence data. The age-standardised consultation rates for "otitis media and earache" in 2006 are: 48.2 per 1000 patients per year (female); 36.8 (male) and proportions of consultations with antibiotics prescribed were: 74.9% (female) and 69.1% (male). This paper suggests that consultation rates decreased over time (the earliest reported year is 1997 when the rates were 57.6 for females and 47.7 for males). Other studies present data for overall population. The most recent data for primary care came from Royal College of GPs Annual Report for 2010. According to this report, the incidence of primary care consultations for OM clinical diagnosis is 27,112.16721 per 100,000 infants (<1 year old).	The UK GPRD is considered large dataset covering primary care diagnosis and consultations in the UK. A study by Hansell et al. (1999) compared the findings from GPRD with the 4th Morbidity Survey in General Practice (MSGP4) and found that "GPRD appears to be valid for primary care epidemiological studies by comparison with MSGP4 and offers advantages in terms of large size, a longer time period covered, and ability to link prescriptions with diagnosis". There have been some issues around missing data and miscoding of diagnoses.	The RCGP data is the most up-to-date, is based on 105 practices across England (regional health authority representation of 0.66% in East of England to 2.56% in London) although it is based on weekly reports and therefore is not free from double counting if two different Read codes are entered within the same week. The extent of this bias is now known.

Unit cost of primary care consultation	Curtis (2010)	This is the most widely used and robust source for unit cost in health and social care. Per surgery consultation lasting 11.7 minutes is estimated at £36 with qualifications costs (£32 without it) and includes direct care staff costs. The estimation builds on assumptions like remuneration, qualification costs, ongoing training, capital costs, overhead, travel and working time. The per-surgery consultation minutes are based on "The Information Centre (2007) 2006/07 UK General Practice Workload Survey, Primary Care Statistics, The Information Centre, Leeds." This book also provides different estimates based on where the GP consultation took place, e.g. surgery (£36), clinic (£53), telephone (£22), and home visit (£122). For the current analysis, the cost of surgery-consultation is used as conservative estimate. All prices are 2009-10.	Most obvious source of data for GP unit costs.	Relevant.

Reviewed sources for parameters in necrotising enterocolitis model

Input parameter	Source	Description from the source (summarised if necessary)	Comments	Extent of relevance to our work
Births	ONS 2009	The total UK population is 61792000 in 2009 and ONS estimates that the live birth rate is 12.8/1000. This means the total number of live birth in 2009 in the UK is 790,938 (61792000*12.8/1000).	These are the most recent data on birth and deaths available from the Office for National Statistics and regarded as the most relevant.	Relevant as the reference population in this study is all infants born in the UK who are admitted to neonatal units in the given year. In order to apply the admission rates, this population is required.
Neonatal admissions rate	Macfarlane et al. (2001) and Redshaw & Hamilton (2006)	Two sources of data exist to support a rate of 10% of all babies being admitted to Neonatal Units. Macfarlane A et al. Birth Counts. Statistics of pregnancy and childbirth. Second Edition 2001, which estimated the rate to be about 10% in all four countries of the UK in 1995/96. Redshaw and Hamilton (2006) estimated that there were a total of 74,510 neonatal admissions in the UK. The figures were based on "the responses to the surveys with additional information about admissions for non-respondents utilising the Directory of Critical Care". When compared with the total number of live births in that year, it turns out that the rate is about 10%.	These figures are based on actual number of admissions in all four countries in the UK and therefore are the most comprehensive.	Relevant as it is based on actual recorded data in the United Kingdom

Breastfeeding rates	Bonet et al. (2010)	This European Study, called MOSAIC which does include UK, compared breastfeeding rates at discharge for very pre-term infants between neonatal units. This is a population based cohort of 3006 very preterm births (22-31 weeks of gestation) discharged home from neonatal units in 8 European countries. Data on maternal and infant characteristics were obtained from medical records using a common protocol. Data were from 2003. Feeding at discharge was recorded as breastmilk, formula or mixed. Infants were considered 'breastfed' if they were fed exclusively or partly breast milk. The type of feeding at discharge was known for over 95% of infants. The study went further and modelled, using multi-level modelling techniques, the likelihood of breastfeeding. The control variables included maternal characteristics such as mother's age, parity and country of birth and child characteristics such as gestational age, sex, multiple birth, small for gestational age, Apgar score, congenital anomaly, etc. The neonatal unit control variables included level of care, number of admissions and regions. The Trent region of the United Kingdom was included in the study (n=591 infants). The breastfeeding rate in the UK therefore was estimated at 29% at discharge. This is the % of babies in the neonatal units who were breastfed or had breast milk.	This is one of the few studies that provide population based data on feeding in neonatal units. The response rate on feeding is high (>95%) and this is a recent peer reviewed publication. The figures from Infant Feeding Survey 2005 are not deemed relevant here as the babies at risk of NEC will be 'very' preterm and 'very' low birth weight and will typically have a long stay in the neonatal unit. For example, in the Henderson (2009) UK case-control study, the median gestational age of the NEC cases was 28 weeks. The Infant Feeding Survey data refers to breastfeeding practice when the respondent mothers' babies were admitted to neonatal units, as opposed to breastfeeding practice in neonatal units.	Relevant as it provides recent data on feeding at neonatal units, particularly in the population that is at risk of NEC. No other obvious source, e.g. Infant Feeding Survey, is deemed relevant.

Odds ratio in favour of breastfeeding on NEC	WP 1 (Renfrew et al.) and WP 2 (Quigley) of the current project	Three studies were identified as candidates for RR measures. Study1 - Quigley et al 2007, Cochrane systematic review compares several outcomes in babies who received donor breast milk (DBM) compared with formula milk. 5 RCTs analysed confirmed NEC: 3 of the included trials compared DBM and formula milk where both were given as a sole diet (Analysis 4.04 in the Cochrane review). The comparison is between "exclusive breast milk" with "exclusive formula milk". 2 of the included trials compared DBM and formula milk where both were given as a supplement to mother's own milk (Analysis 5.05 in the Cochrane review). The comparison groups are not relevant to our study: "mother's milk and DBM" (=exclusive breast milk) and "mother's milk and formula" (=breast and formula). The OR in favour of DBM is 0.25 (0.06-0.98). Study 2 – Lucas and Cole 1990, UK study, is based on the combined data from two Lucas RCTs of DBM versus formula which were included in the Cochrane review above. The analysis is not based on the randomised groups, but instead is based on three non-randomised enteral feed groups: human milk only (donor or donor plus mother's milk), formula (term or preterm) as a supplement to mother's milk, and formula only. The OR in favour of formula only is 10.6 (3.0-37.3). Study 3 – Henderson 2009, UK case-control study compared the frequency of expressed BM feeding in 53 cases and 5 matched controls. The NEC cases were classified using Bell stages I/III (13 were stage I and 40 were stage II/III) and 21 cases were confirmed. The OR is 0.32 (0.11-0.98) for received breast milk across stage I/III and 0.19 (0.05 to 0.73) across stage II/III.	These RR are based on systematic reviews and synthesis undertaken as part of the current project (WP1 and WP2). This is based on the best available data reported from UK as well as industrialised countries similar to the UK. The RR comes from a UK case-control study (Henderson et al. 2009). This study was chosen because: a) This study is based on more recent data and hence will be more representative of recently born preterm/LBW babies and current neonatal practice; b) It compares any breast milk with formula; c) It is based on a larger number of NEC cases (53 compared with 10 in the Cochrane review) even though the total sample size is smaller (n=106 compared with 305 in the Cochrane review). Some babies in these studies are likely to have received breastmilk fortifier.	Relevant as agreed by the research team.

Incidence of NEC	HES Online data 2009-10, Information Centre	There were 677 Finished Consultant Episodes recorded for "P77: Necrotising Enterocolitis of fetus and newborn" in 2009-10 in Hospital Episode Statistics in England. The ONS population statistic for live births in that year is 671,058. Assuming 10% of this newborn population would have neonatal admissions, 677 cases of NEC means an incidence rate of 1%.	This is the best available data as it captures ALL care episodes of NEC in England. Estimating incidence of NEC for the UK based on this English data is deemed more appropriate than estimating incidence based on another UK prevalence study (Rees et al. 2010) as their data come from a 51% response rate and focus only on level 2 and level 3 units only.	Relevant as it is based on actual recorded data in England.
Incidence of NEC	Rees et al. 2010	This is the most recent study that provides epidemiological estimates on NEC cases. However, the reported figures are prevalence and the data was collected over 2 winter and 2 summer months from a sample of 158 level 2 and 3 neonatal units in 2005 and 2006, following a prospective cross-sectional survey design. The response rate was 51%. The study suggests there is an overall risk of 2% in all NICU babies; a risk of 14.4% in those with birthweight < 1000 g; and a risk of 13.8% in those with gestation <26 weeks a risk of 10.8% in those with gestation 26-28 weeks. Despite low response rate, the estimates on this study reflect the policy and care contexts of the UK, unlike studies from elsewhere. Also, as NEC is very serious, often fatal it is unlikely that any babies would have appeared more than once in the study- so treating this prevalence as if it was incidence is reasonable. As a cross check how this figure compares: Sullivan et al. (recent US data in those with birth weight 500 to 1250 g): 3/67=4.5% (for mother's milk plus donor breast milk) 5/71=7% (for mother's milk plus donor breast milk) 11/69=15.9% (for mother's milk plus formula). If we assume that the UK figure of 14.4% in those with birthweight <1000 g includes babies from all feeding groups (exclusive BM, mixed feeding, exclusive formula) then this is very similar to the US figure of 15.9% in those with birthweight 500-1250g who received mixed feeding. An old report (11th BPSU Annual Report	There are two potential problems with this data: they are related to level 2 and 3 neonatal units only and the overall response rate on which the estimates are based on is just 51%. Because actual recorded numbers of NEC episodes across all neonatal units are available via Hospital Episode Statistics, the figure of Rees et al. may overestimate the true costs.	Only relevant if we are to focus on level 2 and 3 neonatal units. May be good for sensitivity analysis

		1996-97) also suggests that "The estimated incidence of confirmed NEC was 0.23 per 1000 live births, increasing to 2.1 per 1000 neonatal unit admissions." However, they suggest that this could be an underestimation and conclude, "the estimated incidence of confirmed NEC would rise to 0.30 per 1000 live births and 2.7 NICU admissions".		
Unit cost of a NEC diagnosis and treatment	HES Online data 2009-10, Information Centre	The HRG procedure, "PB01Z: Major neonatal diagnosis" can be used to reflect the diagnosis and treatment, including surgery, of a NEC case. This is a population average and includes those babies who died following a NEC treatment.	No unit cost data on a NEC case exist. Previous studies, including a recent one that evaluates breastfeeding support intervention (Renfrew et al. 2009 and Rice et al. 2010) have assumed that the cost of an NEC illness episode is closest to a major neonatal diagnosis quoted in the NHS Reference costs. No mapping exist for ICD-10 code P77 (necrotising enterocolitis of fetus) from both HRG4 and HRG3.5. However, according to HRG3.5, the ICD-10 condition "P781: other neonatal peritonitis" (a surgical procedure done on NEC cases) is “N01: Neonates - Died <2 days old, used where a primary diagnosis requires a short stay and the presence of the ‘died’ indicator to correctly group” OR “N05: Neonates with one Major Diagnosis, the base HRG to which the procedure or diagnosis code is grouped	Relevant as it comes directly from HRG (most obvious source of such data).

			when all other exception logic has failed". Based on the above, it is reasonable to assume that the HRG4 code (PB01Z: Major Neonatal Diagnoses in the new HRG) is the most appropriate proxy for NEC treatment costs per case. It does not cover, however, the in-patient stays in neonatal units.	
Unit cost of in-patient stay in neonatal units	HES Online data 2009-10, Information Centre	Weighted average of the following codes: XA01Z: Neonatal critical Care Intensive Care; XA02Z: Neonatal Critical Care High Dependency; XA03Z: Neonatal Critical Care Special Care without external carer; XA04Z: Neonatal Critical Care Special Care with external carer; XA05Z: Neonatal Critical Care Normal Care. Note that this is population average and includes the stays of those who died.	This is the weighted average of in-patient stays in neonatal units, expressed as unit cost of a bed day.	Relevant as it comes directly from HRG (most obvious source of such data).
Mean length of stay in neonatal units	HES Online data 2009-10, Information Centre	Hospital Episode Statistics for England, 2009-10 ICD-10 code- P77: Necrotizing enterocolitis of fetus and newborn suggests that the mean length of stay was 26.70 days with median LOS of 12 days. Note that this is population average and includes those who died.	Actual data on LOS in England. It is reasonable to assume the same average applies to the entire United Kingdom. The average LOS is smaller compared to Bisquera et al because this includes all neonatal units and not only higher levels.	Relevant as it comes directly from HES (most obvious source of such data).

Mean length of stay in neonatal units	Bisquera et al. (2002)	This widely referred case-control study, reported from the US, examined the length of stay in 2 neonatal intensive care units in an academic medical centre. The sample included infants born 1992-1994 with birthweight <1500g. Out of 866 infants admitted over 2 years, 10% (86) developed NEC. The average LOS reported are as follows: 95+/-42 days for medical NEC survivors; 142+/-65 days for surgical NEC survivors; 60 +/-45 days for medical NEC non-survivors and 48+/-30 days for surgical NEC non-survivors.	This is a small scale study and focussed only on intensive care units. Therefore, a much greater LOS compared to HES data is understandable.	Not relevant as UK specific data across all neonatal units is available.

Reviewed sources for parameters in maternal breast cancer model

Input parameter	Source	Description from the source (summarised if necessary)	Comments	Extent of relevance to our work
Mean age at first birth	ONS 2009	This figure (28 years) comes from ONS statistics on maternity and births	The most obvious source of data	Relevant as these are based on census data analysis/projections
Average age at onset of breast cancer	Cancer Research UK Statistics	Estimated based on Cancer Research UK statistics on new cases of breast cancer 2006-2009. The data are provided according to age band and number of newly diagnosed cases, which allowed us to estimate mean age at onset (68 years)	The best available data to use	Relevant as this is based on all newly diagnosed cases in the UK.
Number of primiparous births in one year	Euro Peristat	Estimated (313,817) by multiplying the number of live births (788,486) in the UK (ONS 2009) by proportion of primiparous women (39.8%) in the UK (EURO-PERISTAT Project, 2008).	The best available data to use	Relevant as the model requires a cohort of first mothers.

Breastfeeding rates	Liu et al. (2009)	The Million Women Study estimates that 32% parous women never breastfeed, 36% breastfeed for ≤6 months, 16% breastfeed for 7-18 months and another 16% breastfeed for 18+ months. These estimates are cumulative over all children the women had and over her lifetime. The Million Women Study is a prospective study that recruited 1.3 million middle-aged women mostly aged 50–64 years-old through National Health Service (NHS) breast screening centres in England and Scotland during 1996–2001. Women completed a baseline questionnaire on entry to the study	Table 3 provides data for the following estimates: Total parous women (%): Never BF: 292 675 (32.2%); BF < 6 months: 322 897 (35.5%); BF 6-11 months: 142 768 (15.7%); BF >12 months: 150 074 (16.5%); Total women: 908 414.	Relevant. It is the best source of data for estimating cumulative months of breastfeeding - unlike other outcomes, this outcome needs the duration of time the mother has breastfed for, rather than the amount of time the baby has fed for, so the Infant Feeding Survey is not relevant here.
Relative risks in favour of breastfeeding on breast cancer	WP 1 (Renfrew et al.) and WP 2 (Quigley) of the current project	The WP1 and WP2 in the project estimated the relative risks in favour of breastfeeding as follows: never (1.0), less than 6 months (0.98), 7-18 months (0.94), 19-30 months (0.89), 31-54 months (0.88), 55+ months (0.73). Data were available on 50,302 women with breast cancer and 96,973 women without breast cancer. Here, breastfeeding duration represents her total duration summed over all her children. The "never breastfed" group were chosen as the baseline and the highest duration is 55+ months. Table 1 also shows the median duration of breastfeeding in each group. The RRs are adjusted for study, age, parity, age at first birth and menopausal status.	These figures are agreed by the research team and therefore considered to be robust.	Relevant as the huge sample size in the meta-analysis makes it more robust that individual UK studies which are part of the meta-analysis.
Lifetime risk of breast cancer	Cancer Research UK analysis based on ONS data	The Cancer Research UK has estimated the lifetime risk of breast cancer in all four countries of the UK based on ONS data. This relates to ICD code C50 and is the average of three years 2006-2008. The lifetime risk has been estimated to be 1 in 8.	This data is the most recent pooled figure for all countries based on cancer registers and provided by national statistics offices. Therefore, it is the most obvious source so far as the incidence rates are concerned.	Relevant as the data come from all records in the Cancer Registries.

Breast cancer survival rates	Cancer Research UK analysis	Based on the figures from ONS, the Cancer Research UK estimates breast cancer survival rates at 5, 10, 15 and 20 years for women diagnosed in England 2001-2003. Over then ten year period 1991-93 v 2001-03, survival improved for all age-groups at all end-points but the younger women had smaller improvements than women aged over 50 8. For example, ten-year relative survival increased by 13% over this period for women aged 15-49 compared with 24% for women aged 50-69 and 18% for women aged 70 to 99. The 20 year predicted survival rates are: 15-49 years (64%), 50-69 years (72%) and 70-99 years (59%).	As these figures are based on ONS statistics, they are comprehensive (as opposed to figures based on one study). The survival here is 'relative' meaning it captures the 'net survival' among breast cancer patients.	Relevant as they are based on the analysis of survival data based on all cases in the United Kingdom.
Breast cancer survival rates	HTA report: Robertson et al. (2011)	In the most recent HTA report on clinical and cost-effectiveness of different surveillance mammography regimens after the treatment of primary breast cancer, a number of mortality estimates are provided. Table 31 (p. 83) mentions the following 10 year mortality rates: risk profile 1 (4.86%), risk profile 2 (12.47%), risk profile 3 (21.19%), risk profile 4 (36.81%) and risk profile 5 (57.28%). These figures are estimated based on West Midlands Cancer Intelligence Unit's breast cancer registry data.	Although the mortality estimates provided in this report is robust and most recent, they are reported according to stages of cancer and the health states covered in their Markov model developed for screening. These figures do not readily translate to the figures we would need in this analysis, i.e. average survival rates according to three age bands (15-49; 50-69; 70+) irrespective of cancer stages.	Not relevant as these are stage-specific mortality rates. In the presence of relative survival rate (population average by three age-band-see above), these are not considered relevant here.
Annual probability of death in breast cancer cases	Estimated using survival data from Cancer Research UK and ONS Life Table	Adjusted average annual death of dying for the three age-bands (15-49; 50-69: 70+) from the Life Table by relative survival rates.	This is the standard approach to adjust a population average estimate with a relative measure. Verified by MQ	Relevant as the data come directly from Life Table and cancer relative survival

Annual probability of death in general population	ONS Life Table	The ONS Life Table provides annual probability of death by each age.	Because the model used in this research needs annual probability of death by three age bands (15-49; 50-69; 70+), the average probability was estimated by averaging the probabilities across the ages in the relevant band.	Relevant. Given the nature of the model, the average mortality across the three age bands was deemed more appropriate. Verified by MQ.
Average annual costs of treating a breast cancer case	Dolan et al. (1999)	Based on the literature and Cancer Registry data, Dolan et al estimate the average costs of treating cancer in the United Kingdom (all four countries included). These estimates include secondary care (including breast reconstruction to a small proportion of patients), GP visits and palliative care. As these are average across all patients, the reported annual cost per patient includes those who died in this year. Secondary costs (£7072), GP visits (£141), Hospice and nursing/residential care (£34), total (£7247) per patient per year in 1995/96 prices. The estimates cover a total of 33546 breast cancer cases.	This is the most comprehensive study covering all four countries, all stages of cancer and all types of care. The average costs relate to all breast cancer cases and therefore is suitable for the type of model planned for this study. The weakness of this data is that the current treatment pattern may be different from those in place when the study was carried out (1995-96).	Relevant as these are population average. Remak & Brazil (2004) estimated the stage-4 breast cancer costs in the UK at £12,502 and concluded that these figures were comparable with Dolan estimate when inflated. Therefore, as Dolan estimate provide population average, they are deemed relevant.
Average annual costs of treating a breast cancer case	Wolstenhome et al. (1998)	Based on a detailed examination of 137 breast cancer cases treated in the Trent region, this study estimates the secondary costs of treating a breast cancer. The reported annual costs per patient are: £ 3576 (stage 1), £3996 (stage 2), £3916 (stage 3) and £6590 (stage 4) in 1991 pounds.	These estimates are for secondary care only and have been updated by Dolan et al. (1998) in their comprehensive estimates.	Not relevant as these are partial costs and also these estimates have been updated by Dolan et al.

Breast cancer survival rates	HTA report: Robertson et al. (2011)	In the most recent HTA report on clinical and cost-effectiveness of different surveillance mammography regimens after the treatment of primary breast cancer, a number of costs estimates are provided. They are divided as costs of tests (e.g. Clinical examination by GP or consultant, mammogram), costs of invasive tests and treatment (biopsy, mastectomy, chemo, etc.), and costs of surveillance regimen (screening).	As this is the most recent HTA report, we would expect these costs to be robust and most updated. However, using these ingredient costs would require either a full Markov model or the type of model being planned but with more epidemiological information such as proportion of patients needing different tests and treatments. Given Dolan et al (1999) estimates, the value added of this approach is questionable so far as the simple model being planned for this study is concerned.	Not relevant as these are health-state specific mortality rates and not average across the age-bands.
Discount rate	NICE	NICE recommends than a rate of 3.5% should be used to discount the future stream of costs and health effects	NICE recommended discount rate is the one to use in this calculation. However, this rate can be varied in sensitivity analysis.	Relevant as this is recommended by NICE.
Utility	Robertson et al. (2011)	Table 38 provides a number of utility values according to severity and whether or not managed (on or after treatment) or unmanaged. Both high and low values are reported. These values come from a systematic review of breast cancer utilities (Brennan & Wolowacz, 2008- an ISPOR poster). Robertson et al. used the figures reported in this poster to estimate the utilities for five severity levels. The mean of low-value across all reported estimates is 0.67241 and median 0.71165.	As the original study (Brennan & Wolowacz) is a poster with little information, the analysis by Robertson et al. in the most recent review is considered to give a wide range of values across different stages. The median is regarded to give a reasonable population average value.	Relevant as this data comes from a systematic review that summarises the values reported in 9 different studies- some of the included studies are from the UK. To be subject to sensitivity analysis.

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Appendix 10

Policy scenarios modelled and key parameters used for five disease outcomes

Outcome	Modelling technique	Definition of breastfeeding	Policy scenarios for which cost-savings were modelled	Odds ratios in favour of breastfeeding	Incidence	Baseline unit costs (2009/10 prices)
Gastroenteritis (infants)	Incidence-based; first year of life; annual costs	A0: Exclusive breastfeeding (EBF) rate at 4 months (7%) B0: Exclusive breastfeeding (EBF) rate at 6 months (0.5%) C0: 'any breastfeeding' rate at 6-month (25%)	A1: increase rate of EBF at 4 months to rate at 6 weeks (21%) A2: increase rate of EBF at 4 months to rate at 1 week (45%) A3: increase rate of EBF at 4 months to rate at birth (65%) B1: increase rate of EBF at 6 month to rate at 4-months (7%) C1: increase rate of 'any breastfeeding' at 6-months to rate at 6-weeks (48%)	Exclusive breastfeeding: Hospitalisation: 0.39 (0.18-0.85) GP visits: 0.28 (0.11-0.69) Any breastfeeding: Hospitalisation: 0.52 (0.30-0.87) GP visits: 0.36 (0.18-0.74)	Hospital admissions: 17.2/1000 live births Primary care consultations: 4,682/100,000 infants <1 year	<u>Hospital admissions</u>: Baseline: £989 per admitted child Lower quartile: £586 Upper quartile: £1,206 <u>Primary care consultation</u>: Baseline: £36 per GP consultation Upper end cost: £53
Lower respiratory tract infection (infants)	Incidence-based; first year of life; annual costs	A0: Exclusive breastfeeding (EBF) rate at 4 months (7%) B0: Exclusive breastfeeding (EBF) rate at 6 months (0.5%) C0: 'any breastfeeding' rate at 6-month (25%)	A1: increase rate of EBF at 4 months to rate at 6 weeks (21%) A2: increase rate of EBF at 4 months to rate at 1 week (45%) A3: increase rate of EBF at 4 months to rate at birth (65%) B1: increase rate of EBF at 6 month to rate at 4-months (7%) C1: increase rate of 'any breastfeeding' at 6-months to rate at 6-weeks (48%)	Exclusive breastfeeding: Hospitalisation: 0.70 (0.49-0.98) GP visits: 0.69 (0.47-1.0) Any breastfeeding: Hospitalisation: 0.67 (0.52-0.88) GP visits: 0.65 (0.43-0.96)	Hospital admissions: 59.1/1000 live births Primary care consultations: 23,433/100,000 infants <1 year	<u>Hospital admissions:</u> Baseline: £1,078 per admitted child Lower quartile: £749 Upper quartile: £1290 <u>Primary care consultation</u>: Baseline: £36 per GP consultation Upper end cost: £53
Otitis media (infants)	Incidence-based; first year of life; annual costs	A0: Exclusive breastfeeding (EBF) rate at 4 months (7%) B0: Exclusive breastfeeding (EBF) rate at 6 months (0.5%)	A1: increase rate of EBF at 4 months to rate at 6 weeks (21%) A2: increase rate of EBF at 4 months to rate at 1 week (45%) A3: increase rate of EBF at 4 months to	Exclusive breastfeeding: GP visits: 0.50 (0.37-0.70) Any breastfeeding: GP visits: 0.40 (0.21-0.76)	Primary care consultations: 136/100,000 infants <1 year	<u>Primary care consultation</u>: Baseline: £36 per GP consultation Upper end cost: £53

		C0: 'any breastfeeding' rate at 6-month (25%)	rate at birth (65%) B1: increase rate of EBF at 6 month to rate at 4-months (7%) C1: increase rate of 'any breastfeeding' at 6-months to rate at 6-weeks (48%)			
Necrotising enterocolitis (infants)	Incidence-based; during the stay in neonatal units; annual costs	Policy D0: Any breastmilk feeding rate at discharge in neonatal units (35%)	Policy D1: increase rate of any breastmilk feeding at discharge in neonatal units to 50% Policy D2: increase rate of any breastmilk feeding at discharge in neonatal units to 75% Policy D3: increase rate of any breastmilk feeding at discharge in neonatal units to 100%	Any breast milk: 0.19 (0.05-0.73)	NEC cases: 1/100 neonatal admissions Surgical NEC: 31% Medical NEC: 69% Average length of stay: 26.7 days	<u>Surgery:</u> Baseline: £1,450 per episode Lower quartile: £689 Upper quartile: £1,802 <u>Neonatal unit stay</u>: Baseline: £618 per bed-day Lower quartile: £509 Upper quartile: £712
Breast cancer (maternal)	Incidence-based; 20 years from now; annual costs	Policy E0: 32% primiparous women never breastfeeding; 36% breastfeeding for ≤6 months; 16% breastfeeding for 7-18 months; 16% breastfeeding for 18+months	Policy E1: Increase rate of breastfeeding for ≤6 months to 52% 16% never; 52% ≤6 mo; 16% 7-18 mo; 16% 18+ mo Policy E2: Increase rate of breastfeeding for ≤ 18 months to 32% 16% never; 36% ≤6 mo; 32% 7-18 mo; 16% 18+ mo Policy E3: Increase rate of breastfeeding for 18+ months to 32% 16% never; 36% ≤6 mo; 16% 7-18 mo; 32% 18+ mo	Ever breastfeeding vs. never breastfeeding: 0.96 (0.92-0.99) Breastfeeding for <6 months vs. never: 0.98 (0.95-1.01) Breastfeeding for 7-18 months vs. never: 0.94 (0.91-0.97) Breastfeeding for 18+ months vs. never: 0.89 (0.84-0.94)	Breast cancer cases: Lifetime incidence of 12,500/100,000 population (that is a lifetime risk of 1 in 8)	<u>Breast cancer average</u>: Baseline: £11,726 per case Upper end cost: £16,260

Appendix 11

Data extraction tables for included systematic reviews and UK studies: ordered by outcome

Summary list of studies

Bold indicates primary (1^{ry}) source
Italic indicates corroborative study

		Design SR/UK	
1.	**Collaborative Group 2002**	**SR**	**Breast cancer as maternal outcome of not breastfeeding: primary source of data**
2.	*Bernier et al 2000*	*SR*	*Breast cancer as maternal outcome of not breastfeeding: corroborative study*
3.	*Lipworth et al 2000*	*SR*	*Breast cancer as maternal outcome of not breastfeeding: corroborative study*
4.	*Ma et al 2006 (SR)*	*SR*	*Breast cancer as maternal outcome of not breastfeeding: corroborative study*
5.	*Yang and Jacobsen 2008*	*SR*	*Breast cancer as maternal outcome of not breastfeeding: corroborative study*
6.	**Quigley et al 2006**	**UK**	**Gastrointestinal infection as child outcome of not breastfeeding: primary source of data**
7.	**Quigley et al 2007/9**	**UK**	**Gastrointestinal infection as child outcome of not breastfeeding: primary source of data** **Respiratory tract infection as child outcome of not breastfeeding: primary source of data**
8.	*Howie et al 1990*	*UK*	*Gastrointestinal infection as child outcome of not breastfeeding: corroborative study* and **Respiratory tract infection as child outcome of not breastfeeding: primary source of data**

9.	**Fisk et al 2011**	**UK**	*Gastrointestinal infection as child outcome of not breastfeeding: corroborative study* and **Respiratory tract infection as child outcome of not breastfeeding: primary source of data** and **Otitis media as child outcome of not breastfeeding: primary source of data**
10.	*Baker 1998*	*UK*	*Gastrointestinal infection as child outcome of not breastfeeding: corroborative study*
11.	*Kramer & Kakuma 2002*	*SR*	*Gastrointestinal infection as child outcome of not breastfeeding: corroborative study* *and* *Respiratory tract infection as child outcome of not breastfeeding: corroborative study*
12.	**Ip et al 2007/9**	**SR**	*Respiratory tract infection as child outcome of not breastfeeding: corroborative study* (repeats Bachrach 2003, see # 13 below) and **Otitis media as child outcome of not breastfeeding: primary source of data** and *Necrotising enterocolitis (NEC) as outcome of not breastfeeding for babies in intensive (NICU) or special care baby units (SCBU): corroborative study*
13.	*Bachrach et al 2003*	*SR*	*Respiratory tract infection as child outcome of not breastfeeding: corroborative study*
14.	**Henderson et al 2009**	**UK**	**Necrotising enterocolitis (NEC) as outcome of not breastfeeding for babies in intensive (NICU) or special care baby units (SCBU): primary source of data**
15.	*McGuire et al 2003*	*SR*	*Necrotising enterocolitis (NEC) as outcome of not breastfeeding for babies in intensive (NICU) or special care baby units (SCBU): corroborative study*
16.	*Quigley et al 2007*	*SR*	*Necrotising enterocolitis (NEC) as outcome of not breastfeeding for babies in intensive (NICU) or special care baby units (SCBU): corroborative study*

17.	*Lucas et al 1990 (in Quigley et al 2007)*	*UK*	*Necrotising enterocolitis (NEC) as outcome of not breastfeeding for babies in intensive (NICU) or special care baby units (SCBU): corroborative study*
18.	**Horta et al 2007**	**SR**	**Obesity as baby/child outcome of not breastfeeding: primary source of data**
19.	*Armstrong Lancet 2002*	*UK*	*Obesity as baby/child outcome of not breastfeeding: corroborative study*
20.	*Li 2003*	*UK*	*Obesity as baby/child outcome of not breastfeeding: corroborative study*
21.	*Reilly 2005*	*UK*	*Obesity as baby/child outcome of not breastfeeding: corroborative study*
22.	*Wilson 1998*	*UK*	*Obesity as baby/child outcome of not breastfeeding: corroborative study*
23.	**Hauck et al 2011**	**SR**	**Sudden Infant Death (SIDS) as baby outcome of not breastfeeding: primary source of data**
24.	**Quigley et al 2012**	**UK**	**Cognitive outcomes in children who had been born at term, and in children who had been admitted to intensive (NICU) or special care baby units (SCBU), of not breastfeeding: primary source of data**
25.	*Iacovou et al 2010*	*UK*	*Cognitive outcomes in children who had been born at term, and in children who had been admitted to intensive (NICU) or special care baby units (SCBU), of not breastfeeding: corroborative study*

1) Breast cancer as maternal outcome of not breastfeeding: primary source of data

Collaborative Group on Hormonal Factors in Breast Cancer (2002) Breast cancer and breast feeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50,302 women with breast cancer and 96,973 without the disease. The Lancet Vol 360 July 20 pp187-195.	
Objective	To examine the relation between breastfeeding and breast cancer
Design	Collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries. Case control and cohort studies with data for at least 100 women with incident invasive breast cancer, that had recorded information on reproductive factors and use of hormonal preparations for each women, were included
Data collection	A thorough search is reported. So that analyses could be done with as similar definitions across studies as possible, individual patient data were collated from principal investigators of the included studies and analysed centrally
Setting	30 countries from throughout the world
Participants	50,302 women with breast cancer and 96,973 without the disease
Exposure	Any breastfeeding/ no breastfeeding for each child Duration of breastfeeding for each breastfed child (months) Woman's lifetime duration of breastfeeding (total months)
Measure of effect	Relative risks (RR) and standard errors (SE or FSE) Reduction in RR of breast cancer per 12 months breastfeeding reported for each study; all cohort studies; all case-control studies with population controls; all case-control studies with hospital controls; and all studies
Adjustment for confounders	Age, menopausal status, ethnic origin, number of births, age at birth of first child, education, family history of breast cancer, age at menarche, height, weight, BMI, and use of hormonal contraceptives, alcohol and tobacco
Outcome, Significance	• In the absence of breastfeeding, each birth reduced the RR of breast cancer by 7% (95% CI 5.0 to 9.0; p<0.0001). At each parity the RR of breast cancer was slightly lower for women who had breastfed compared with women who had not • RR of breast cancer declined with increasing duration of breastfeeding by 4.3% (95% CI 2.9 to 5.8; p<0.0001) for every 12 months of breastfeeding (in addition to the 7% for each birth) • The size of the decline in the RR of breast cancer associated with breastfeeding did not differ significantly for women in developed (4.1%, SE 1.1) and developing (4.8%, SE 1.3) countries • Adjustment for each of the confounders above did not materially alter the magnitude of the effect of breastfeeding on the RR of breast cancer
Author's conclusion	The longer women breastfeed the more they are protected against breast cancer. The lack of or short lifetime duration of breastfeeding typical of women in developed countries makes a major contribution to the high incidence of breast cancer in these countries.
Comment	

2) Breast cancer as maternal outcome of not breastfeeding: corroborative study

Bernier et al (2000) Breastfeeding and risk of breast cancer: a meta-analysis of published studies. Human Reproduction Update Vol 6 No 4 pp 374-386	
Objective	To evaluate the relation between breastfeeding and breast cancer
Design	Systematic review of case control and prospective cohort studies; addressing risk factors for breast cancer; incorporating history of breastfeeding as a specific variable; specific odds ratio (OR) measuring the breastfeeding and breast cancer association reported or could be derived; published 1980-1998 in English or French Studies in which data from parous women who had not breastfed could not be separated from nulliparous women were excluded
Data collection	Search of Medline and Embase 1980-1998 “breast neoplasms” or “mammary neoplasms” and “breastfeeding”, “lactation” or “prolonged lactation”. Data extraction processes not described
Setting	The 23 included case-control studies were sited in Estonia (1), Canada (2), USA (9), Sicilia (1), Costa Rica (1), Australia (1), India (1), China (1), Mexico (2), Greece (1), Italy (1) and New Zealand (1). One study is described as ‘multicentre’
Participants	9/23 studies recruited cases and controls in hospitals (one of these also had community-based controls). 14/23 studies identified cases from registries and selected controls from the corresponding communities Number of women in each study is reported
Exposure	Ever /never breastfed Duration of breastfeeding (months) 0-6, 6-12, 12+
Measure of effect	Odds ratios and 95% CIs of breast cancer in relation to ever/never breastfeeding reported for each study and for all studies
Adjustment for confounders	12/23 studies had adjusted ORs for one or more of the following factors: age at diagnosis, age at first full term pregnancy, parity, site of birth/ethnicity, age at menarche, familial history of breast cancer, personal history of benign breast disease, site of residence, age at menopause, status of menopause, BMI, use of oral contraceptives, social category, marital status, alcohol use, physical exercise, educational level, use of hormone replacement therapy.
Outcome, Significance	• Pooled OR of breast cancer for ever/never breastfeeding: fixed effect 0.89 (95% CI 0.85 to 0.83) • Pooled OR of breast cancer for ever/never breastfeeding according to breast cancer diagnosed pre/post menopause: Non-menopausal fixed effect 0.83 (0.77 to 0.90), Menopausal fixed effect 1.01 (0.95 to 1.08) • Pooled OR of breast cancer for ever/never breastfeeding according to duration of breastfeeding: 0-6 months 1.02 (0.96 to 1.09), 6-12 months 0.97 (0.89 to 1.05), 12+ months 0.75 (0.71 to 0.81)
Author’s conclusion	A decreased risk of breast cancer was observed in ever breastfeeding vs never breastfeeding parous women. This decrease was more pronounced in non-menopausal women at the time of diagnosis of breast cancer, and in long-term breastfeeding women. Breastfeeding appeared to be a protective factor but was of small magnitude compared with other known risk factors for breast cancer
Comment	Results were not differentiated by country Total number of participants not reported, appears to be 75,198

3) Breast cancer as maternal outcome of not breastfeeding: corroborative study

Lipworth et al (2000) History of breastfeeding in relation to breast cancer risk: a review of the epidemiologic literature. Journal of the National Cancer Institute Vol 92 No 4 Feb 16 pp 302-312	
Objective	To critically evaluate the existing epidemiologic evidence that history of breastfeeding may decrease the risk of breast cancer
Design	Systematic review of case-control studies with narrative synthesis Inclusion: case-control studies with >200 cases that controlled for number of full-term pregnancies and age at first birth
Data collection	Search of Medline 1966-1998 “breastfeeding” or “lactation” and “breast cancer”
Setting	No country restrictions. Setting of the 27 included studies is noted. Narrative summary of cumulative duration of breastfeeding differentiates between “Western” and “non-Western” societies.
Participants	Women with breast cancer and controls. Selection of controls varied by study and is indicated in tables but not summarised in the paper. Studies whose reference groups included nulliparous women are indicated
Exposure	Measure of exposure differs and is shown for each study. The narrative syntheses discuss ever/ never breastfeeding, number of children breastfed, cumulative duration of breastfeeding, average duration of breastfeeding per child, and reasons for cessation of breastfeeding (insufficient milk, lactation suppressants)
Measure of effect	Odds ratios and CIs are presented for individual studies. Statistical summaries of effect are not presented
Adjustment for confounders	All included studies adjusted for number of full-term pregnancies and age at first birth. Other confounders adjusted for vary widely between studies
Outcome, Significance	No summary statistics
Author’s conclusion	An inverse association between increasing cumulative duration of breastfeeding and breast cancer risk among parous women has been reported in some, but not all studies, therefore inconclusive The failure to detect an association in some Western populations may be due to the low prevalence of prolonged breastfeeding The protective effect, if any, of long-term breastfeeding appears to be stronger among, or confined to, premenopausal women While breastfeeding is a potentially modifiable behaviour, the practical implication of reduced breast cancer risk among premenopausal women with prolonged durations of breastfeeding may be of marginal importance, particularly in Western societies
Comment	Paper states individual results were evaluated for bias, confounding and chance but does not say how

4) Breast cancer as maternal outcome of not breastfeeding: corroborative study

Ma et al (2006) Reproductive factors and breast cancer risk according to joint estrogen [ER] and progesterone [PR] receptor status: a meta-analysis of epidemiological studies	
Objective	To quantitatively summarise studies that have investigated the association among parity, age at first birth, breastfeeding or age at menarche in relation to ER+PR+ and ER-PR- cancer
Design	Systematic review with meta-analysis Inclusion: cohort and case control studies with estimates of relative risk (RR) for ER+PR+ and ER-PR- breast cancer Exclusion: data for the two rare subtypes (ER-PR+ and ER+PR- breast cancer) were not summarised because few studies reported RR for them.
Data collection	Searched Medline 1966-2005 “breast neoplasm/ep [Epidemiology]” and “(ER or PR).mp [mp = title, abstract, name of substance, mesh subject heading”
Setting	No country limitations. The ten included studies were set in US (n=7), and 1 each from Australia, Canada and Japan
Participants	Women of all ages
Exposure	Varies by study: Ever/never breastfed; >6months/never; >6months/never or nulliparous; 12months/never; >12months/never; per 3 months’ increase
Measure of effect	RR and 95% CI are presented for each study Summary RRs for population-based case-control studies, hospital-based case-control studies and all studies are shown for highest versus lowest breastfeeding (exposure) category
Adjustment for confounders	Adjustment for potential confounders is listed and differs between studies
Outcome, Significance	Breastfeeding was associated with reduced RRs of both types of breast cancer: ER+PR+ gave RR 0.95 [95% CI 0.87 to 1.05] and ER-PR- gave RR 0.91 [0.83 to 1.00]
Author’s conclusion	Breastfeeding (and late age at menarche) decreased the risk of both types of breast cancer Breastfeeding (and age at menarche) may act through different hormonal mechanisms than do parity and age at first birth
Comment	Ten included studies, seven studies in the meta-analysis

5) Breast cancer as maternal outcome of not breastfeeding: corroborative study

Yang & Jacobsen (2008) A systematic review of the association between breastfeeding and breast cancer	
Objective	To explore whether a consensus about the relationship between breastfeeding and breast cancer has emerged since Lipworth et al 2000 found 'inconclusive'
Design	Systematic review with narrative synthesis Inclusion: Humans only; any language Exclusion: editorials, letters, case reports, guidelines, comments, reviews, meta-analyses
Data collection	Search of PubMed, 1999-2007, with Mesh terms "breastfeeding" or "lactation" and "breast neoplasms"
Setting	Details of the 31 included studies include their setting, in 18 countries: Brazil, China, Colombia, Egypt, Germany, Iceland, Indonesia, Israel, Italy, Malaysia, Mexico, Nigeria, Pakistan, South Africa, Sweden, Turkey and the US
Participants	Parous and nulliparous women
Exposure	Ever/never breastfed
Measure of effect	Adjusted odds ratio and 95% CI for each included study
Adjustment for confounders	Adjustment and matching differ between included studies and are listed for 27/31 included studies
Outcome, Significance	30 case control studies and one cohort study were included No summary statistics
Author's conclusion	No consensus about the relationship between breastfeeding and breast cancer (2008). Recommended further consideration of possible confounders
Comment	This review does not meet our inclusion criteria. However it describes what was understood in 2008. Collaborative Group on Hormonal Factors in Breast Cancer (2002) (see #1) has changed this understanding

6) Gastrointestinal infection as child outcome of not breastfeeding: primary source of data

Quigley et al (2006) How protective is breast feeding against diarrhoeal disease in infants in 1990s England? A case-control study. Arch Dis Child 2006;91:245–250.	
Objective	To measure the effect of breast feeding on diarrhoeal disease in 1990s England, to determine whether this effect varied by social deprivation, and to assess whether inadequate sterilisation is a risk factor
Design	Case-control
Data collection	Cases and controls, or their guardians, were asked to complete a postal risk factor questionnaire, which included variables on infant feeding, social factors, accommodation, travel, and contact with persons with diarrhoeal disease.
Setting	Thirty four general practices in England
Case/ outcome definition (N) (inclusion/ exclusion)	A diarrhoeal disease case was defined as someone who presented to the GP with loose stools or significant vomiting lasting less than two weeks (n=167; 56 aged under 6 months, 111 aged 6-12 months) Inclusion: aged 1 year or less and had data available on infant feeding; this episode preceded by a symptom-free period of three weeks Exclusion: known non-infectious cause of symptoms
Controls Definition (N) (inclusion/ exclusion, matching)	Controls were selected from the practice's register and had been free of loose stools or significant vomiting for three weeks (n=137; 43 aged under 6 months, 94 aged 6-12 months) Inclusion: aged 1 year or less and had data available on infant feeding; free of loose stools or significant vomiting for three weeks Exclusion: n/a Matching: controls were matched for age and sex
Exposure	Infant feeding was defined as: • current milk feeding (exclusive breast milk, mixed breast/ formula feeding, or exclusive formula) • for formula fed infants, ever/ never breast fed and if ever, for how long • whether the infant was weaned onto solids "Exclusive breast milk" meant that the only milk the infant received was breast milk, although many had been weaned onto solids
Measure of effect	Adjusted odds ratios Population attributable fractions (PAFs) for diarrhoeal disease associated with infant feeding variables were then estimated
Adjustment for confounders	Eligible cases and controls were stratified according to: • age group (0–3 months, 3–5.9 months, 6–8.9 months, >9 months) • Jarman score for the practice (25, 25 to 10, 10) • location of the practice (London, not London) These strata formed the matched sets for conditional logistic regression. Potential confounding factors associated with diarrhoeal disease ($p < 0.10$) were included in a multivariate model where infant feeding was the main exposure. The likelihood ratio interaction test was used to determine whether the effect of infant feeding varied according to: • social class (I–IIInm versus IIIm–V/other) • crowding (<0.7 versus ≥0.7 total persons in house/total rooms) • accommodation type (rented council versus not)

	• Jarman (<1.5 versus ≥1.5, where 1.5 was the median value).
Outcome, Significance	Receiving no breast milk and not receiving exclusive breast milk were both significantly associated with an increase in diarrhoeal disease (adjusted OR=2.74 [95% CI 1.35 to 5.57] and 3.62 [95% CI 1.45 to 9.03] respectively). Stratified matched odds ratios are reported
Author's conclusion	Breast feeding protects against diarrhoeal disease in infants in England although the degree of protection may vary across infants and wear off after breast feeding cessation Education about the benefits of breast feeding and the risks of inadequate sterilisation should be targeted at carers in deprived areas or households
Comment	Primary source of data

7) Gastrointestinal infection as child outcome of not breastfeeding: primary source of data
Respiratory tract infection as child outcome of not breastfeeding: primary source of data

Quigley et al (2007) Breastfeeding and Hospitalization for Diarrheal and Respiratory Infection in the United Kingdom Millennium Cohort Study. *Pediatrics* 2007;119;e837-e842 AND **Quigley et al (2009)** Infant feeding, solid foods and hospitalisation in the first 8 months after birth. Arch Dis Child 2009;94:148–150.	
Objective	To measure the effect of breastfeeding on hospitalization for diarrheal and lower respiratory tract infections (LRTI) in 15, 980 infants who were born in the United Kingdom in 2000–2002
Design	Cohort study (Millennium Cohort Study)
Data collection	Data from interview with parents when most infants were aged 9 months. Data from months 1-8 were included.
Setting	Nationally representative UK sample
Case/ outcome definition (N) (inclusion/ exclusion)	Diarrhea was defined as "gastroenteritis" Inclusion: term, singleton infants who did not have major problems at birth; hospitalised for diarrhoea (n=201) Exclusion: twins and higher order multiples, singleton infants born at <37 completed weeks' gestation, singleton infants born at ≥37 weeks' gestation and were admitted to ICUs at birth, main respondent not natural mother, consent withdrawn, and infant's age missing; hospitalised for "other persistent or severe diarrhea", "other severe or persistent vomiting", "other reflux or other vomiting", "other gastrointestinal abnormalities"
Controls Definition (N)	n/a
Exposure	Infant feeding was categorized per month into the following groups, which refer to the previous month: 1) not breastfed 2) partially breastfed (received some breast milk but also received other milk and/or solids) 3) exclusively breastfed (received only breast milk and no other milk, solids, or fluids other than water)
Measure of effect	Odds ratios (ORs) were estimated using logistic regression. Population-attributable fractions (PAFs) for hospitalization that was associated with not breastfeeding were then estimated as (proportion of cases exposed) X (OR - 1)/OR, where OR is for not breastfeeding compared with exclusive/partial breastfeeding.
Adjustment for confounders	The ORs were adjusted initially for: birth weight, gestation, mode of delivery, infant's age in months, infant's gender, maternal age in years, whether the infant was first-born, maternal (current) smoking, maternal occupation (coded using the United Kingdom National Statistics Socio-economic Class), maternal education, maternal marital status, and whether the infant lives in rented accommodation. In final models, adjustment was made for variables that were significantly (P <0.05) associated with the outcome after adjustment for other variables in the model. Those who were hospitalized for diarrhea were more likely to be hospitalized for LRTI than those who were not hospitalized for diarrhea, but the effect was not statistically significant (OR: 1.63; 95% CI: 0.70–3.81; P=0.26). Therefore, neither infection was considered as a potential confounder for the other infection.

Outcome, Significance	• Seventy percent of infants were breastfed (ever), 34% received breast milk for at least 4 months, and 1.2% were exclusively breastfed for at least 6 months • By 8 months of age, 12% of infants had been hospitalized (1.1% for diarrhea and 3.2% for lower respiratory tract infection) • Data analyzed by month of age, with adjustment for confounders, show that exclusive breastfeeding, compared with not breastfeeding, protects against hospitalization for diarrhea and lower respiratory tract infection • The effect of partial breastfeeding is weaker • Population attributable fractions suggest that an estimated 53% of diarrhea hospitalizations could have been prevented each month by exclusive breastfeeding and 31% by partial breastfeeding • Similarly, 27% of lower respiratory tract infection hospitalizations could have been prevented each month by exclusive breastfeeding and 25% by partial breastfeeding • The protective effect of breastfeeding for these outcomes wears off soon after breastfeeding cessation Re. exclusive milk feeding, Quigley et al (2009) found the monthly risk of hospitalisation: • was not significantly higher in those who had received solids compared with those not on solids (for diarrhoea, adjusted odds ratio 1.39, 95% CI 0.75 to 2.59; for LRTI, adjusted odds ratio 1.14, 95% CI 0.76 to 1.70) • did not vary significantly according to the age of starting solids
Author's conclusion	Breastfeeding, particularly when exclusive and prolonged, protects against severe morbidity in contemporary United Kingdom A population-level increase in exclusive, prolonged breastfeeding would be of considerable potential benefit for public health
Comment	Key paper

8) Gastrointestinal infection as child outcome of not breastfeeding: corroborative study and Respiratory tract infection as child outcome of not breastfeeding: primary source of data

Howie et al (1990) Protective effect of breastfeeding against infection. BMJ, 6 Jan, vol 300, pp 11-16	
Objective	To assess the relations between breast feeding and infant illness in the first two years of life with particular reference to gastrointestinal disease (respiratory illness; ear, eye, mouth, and skin infections; infantile colic; eczema; and nappy rash are also reported)
Design	Prospective observational study of mothers and babies followed up for 24 months after birth
Data collection	Women with singleton pregnancies recruited at 36 weeks' gestation at the antenatal clinic of one hospital in Dundee Infant feeding data from birth and at hospital discharge from hospital records Detailed observations of infant feeding and illness collected during home visits by health visitors on standardised forms at: two weeks; one, two, three, four, five, six, nine, 12, 15, 18, 21, and 24 months
Setting	Community setting in Dundee, Scotland
Case/ outcome definition (N) (inclusion/ exclusion)	Infant illnesses defined as follows: • Gastrointestinal illness: vomiting or diarrhoea, or both, lasting as a discrete illness for 48 hours or more; episodes of vomiting were coded separately from persistent posseting or episodes of regurgitation. • Diarrhoea was diagnosed on the basis of frequent unformed stools; these episodes were distinguished from chronic diarrhoeal disease, such as intolerance to cows' milk or malabsorption, which was coded separately. • Respiratory infections-coryza (head cold), accompanied by cough or wheeze, or both, lasting for 48 hours or more. • Ear infection-painful or discharging ear lasting for 48 hours or more. Inclusion: Women in a stable relationship living in Dundee (750 recruited) Recruited Sep 1983 to Dec1984; Mar-Aug 1985; and Dec 1985 to May 1986 In children with recurring episodes of the same illness a week of good health free from symptoms was required before a new episode of illness was considered to have occurred N=674 available for analysis (618 followed up for two years) Exclusion: Premature birth (<38 weeks), low birth weight (<2500 g), or infant in special care >48 hours
Controls Definition (N)	n/a
Exposure	At each scheduled visit by the health visitor details of the infant feeding in the 24 hours before the visit were recorded On the basis of the infant feeding record mothers were allocated into one of four infant feeding groups 1. Full breast feeders: breast fed for ≥13 weeks, did not introduce supplements before 13 weeks (n=97)

	2. Partial breast feeders: breast fed for ≥13 weeks, introduced supplements before 13 weeks (n=130) 3. Early weaners: started breast feeding, discontinued before 13 weeks (n=180) 4. Bottle feeders: bottle fed from birth (never breastfed) (n=267)
Measure of effect	• Chi-squared tests • Multiple logistic regression to summarise the data by expressing the logarithmic odds of disease incidence as a linear function of the explanatory variables
Adjustment for confounders	In analysis of differences between feeding groups, adjusted for three variables that explained important amounts of variation in the incidence of infant gastrointestinal infection during the first three months: 1. father's social class 2. maternal age 3. either or both parents smoked
Outcome, Significance	During the first 13 weeks of life: • Adjusted rates of gastrointestinal illnesses significantly lower in Groups 1 & 2 combined (full and partial breastfeeders) compared with other infant feeding methods (p<0.001; 95% CI 7.9% to 16.5%) • Adjusted rates of respiratory infection in bottle feeders significantly greater than in partial and full breastfeeders (p<0.05) • No significant differences found between breast and bottle fed infants for the other illnesses studied (eye, mouth, and skin infections; infantile colic; eczema; and nappy rash) After the first 13 weeks of life: • Compared with the bottle fed infants, the infants who had been partially or fully breast fed in the first 13 weeks of life had significantly lower rates of gastrointestinal illness at 14- 26 weeks (p<0 01), 27-39 weeks (p<0 05), and 40-52 weeks (p<001) • No consistent differences were found for respiratory illness; eye, mouth, and skin infections; infantile colic; eczema; or nappy rash)
Author's conclusion	Breast feeding during the first 13 weeks of life confers protection against gastrointestinal illness that persists beyond the period of breast feeding
Comment	Follow up studies of the following outcomes have been published: Wilson et al 1998 - Respiratory illness, weight, height, body mass index, percentage body fat, and blood pressure in relation to duration of breast feeding and timing of introduction of solids Khan et al 2009 - breastfeeding in infancy and vascular function in later childhood

9) Gastrointestinal infection as child outcome of not breastfeeding: corroborative study
and
Respiratory tract infection as child outcome of not breastfeeding: primary source of data
and
Otitis media as child outcome of not breastfeeding: primary source of data

Fisk et al (2011) Breastfeeding and reported morbidity during infancy: findings from the Southampton Women's Survey *Maternal and Child Nutrition* (2011), 7, pp. 61–70	
Objective	To investigate the relationship between breastfeeding duration and reported gastrointestinal, respiratory and ear infection symptoms in a longitudinal birth cohort study in which we are able to adjust for a range of confounding factors, and to examines whether there are protective effects beyond the period of breastfeeding
Design	Longitudinal birth cohort study – the Southampton Women's Survey (SWS)
Data collection	SWS participants with infants were visited by trained research nurses at infant ages 6 and 12 months. A detailed history of milk feeding (human milk, baby formulas and other milks) and of episodes of illness was obtained at both visits. The age at which solids were first regularly introduced was obtained at 6 months.
Setting	The SWS enrolled women who were residents in the city of Southampton, UK
Case/ outcome definition (N) (inclusion/ exclusion)	Maternal report of infant having suffered from any of the following over the previous 6 months: diarrhoea that lasted two or more days (n=317/1761 (18%) from 0-6 months and 613/1719 (36%) at 6-12 months), one or more bouts of vomiting that lasted two or more days, one or more episodes of chest wheezing/whistling or woken at night coughing three or more nights in a row (prolonged cough) Maternal report of infant having been diagnosed by a doctor as having had a chest infection, bronchitis, bronchiolitis, pneumonia or an ear infection over the previous 6 months (n=1764 infants in the analysis) Inclusion: Singleton infants born to SWS women up to the end of 2003 Exclusion: Infants who were born at <37 weeks gestation, neonatal deaths, major congenital abnormalities, no follow-up at 6 or 12 months, and infants for whom data on the age of last breastfeed were missing
Controls Definition (N)	n/a
Exposure	Breastfeeding duration was defined according to date of last breastfeed and therefore included all types of breastfeeding, including mixed feeding (breast milk alongside infant formula and other foods and drinks)
Measure of effect	Adjusted relative risks and 95% confidence intervals
Adjustment for confounders	10 variables that were associated with breastfeeding duration were entered into a multiple regression model that showed that: 1. maternal age 2. smoking in pregnancy 3. educational attainment 4. BMI 5. months that the mother had been back at work

	6. age at which solids were first regularly introduced were all independently associated with breastfeeding duration (all $P < 0.001$) These six variables were considered as potential confounders and were therefore entered as covariates in the subsequent analyses.
Outcome, Significance	The adjusted relative risks and 95% confidence intervals for a breastfeeding duration of six or more months compared with a baseline of 'never breastfed' were: • 0.67 (0.51–0.87) for chest wheezing/whistling • 0.65 (0.43– 0.96) for diagnosed lower respiratory tract infections • 0.57 (0.40–0.81) for prolonged cough • 0.72 (0.58–0.89) for general respiratory morbidity • 0.43 (0.30–0.61) for diarrhoea • and 0.60 (0.39–0.92) for vomiting The corresponding adjusted relative risk for diagnosed ear infections was 0.40 (0.21–0.76), but the trend in the decreased risk of ear infections with increasing breastfeeding duration was not robust to adjustment for confounders Breastfeeding duration between birth and 6 months was not associated with any outcome between 6 and 12 months of infancy after taking account of confounders
Author's conclusion	• A longer duration of breastfeeding was associated with graded falls in gastrointestinal and respiratory morbidity in infancy that were not explained by maternal characteristics including smoking in pregnancy and age at which mother first regularly introduced solids • Although the protective effect of breastfeeding was strongest between birth and 6 months, there were still important benefits seen with increased breastfeeding duration in later infancy, particularly against diarrhoeal infections • The protective effects of breastfeeding on reported gastrointestinal and respiratory morbidity in the community were comparable with earlier estimates based on reported hospital admissions
Comment	

10) Gastrointestinal infection as child outcome of not breastfeeding: corroborative study

Baker et al 1998 (ALSPAC team). Inequality in infant morbidity: causes and consequences in England in the 1990s. *J Epidemiol Community Health* 1998;52:451–458	
Objective	To examine the effect of deprivation, crowding, maternal smoking, and breast feeding on morbidity from wheeze and diarrhoea in the first six months after birth.
Design	Survey – Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC)
Data collection	Maternal responses on self completion questionnaires at 6 months after birth
Setting	The three health districts of Bristol (Avon, UK)
Case/ outcome definition (N) (inclusion/ exclusion)	Mothers were asked “Has your baby ever had diarrhoea or gastroenteritis?” (Yes/No) “How many days did the worst bout last?” Cases were those mothers reported on the 6 month questionnaire
Controls Definition (N) (inclusion/ exclusion, matching)	n/a *Subjects*—8501 infants from ALSPAC, in which all women expecting a baby between April 1991 and December 1992 in Bristol were invited to participate
Exposure	Any breastfeeding Duration of any breastfeeding
Measure of effect	Adjusted odds ratios (95% CI)
Adjustment for confounders	The variables housing tenure, overcrowding, parity, mother’s educational level, breastfeeding and breastfeeding duration were used in a series of logistic regression analyses to assess their association with the prevalence of diarrhoea. Three regression analysis models were used. The third model (model C) included the behavioural variables in addition to the deprivation variables and the crowding variables; this was used to assess the overall effect of the duration of breast feeding and maternal smoking on wheeze and the duration of breast feeding on diarrhoea after adjusting for all four confounding variables.
Outcome, Significance	A higher prevalence of diarrhoea in infancy was associated with living in rented accommodation (OR=1.25, 95% CI = 1.10, 1.41) and lower maternal education (OR=0.76, 95% CI = 0.69, 0.84) and a lower prevalence with breast feeding (OR=0.42, 95% CI = 0.37, 0.48). An episode of diarrhoea was significantly less likely to last for six or more days if an infant lived in mortgaged accommodation (OR=1.34 95% CI = 1.03, 1.75) and was breast fed for three or more months (OR=1.34 95% CI = 1.03, 1.75). (Outcomes for wheeze also reported)
Author’s conclusion	Deprivation was associated with heightened morbidity from wheeze and diarrhoea for this geographical cohort of infants in England in the 1990s. Results supported evidence suggesting that breast feeding is protective against such conditions and is particularly associated with reduced severity and duration.
Comment	Unclear which four variables are the “true confounders”

11) Gastrointestinal infection as child outcome of not breastfeeding: corroborative study
and
Respiratory tract infection as child outcome of not breastfeeding: corroborative study

Kramer MS, Kakuma R. Optimal duration of exclusive breastfeeding. *Cochrane Database of Systematic Reviews* 2002, Issue 1. *(See comment at foot of page about updates)*	
Objective	To assess the effects on child health, growth, and development, and on maternal health, of exclusive breastfeeding (EBF) for six months versus exclusive breastfeeding for three to four months with mixed breastfeeding (MBF; introduction of complementary liquid or solid foods with continued breastfeeding) thereafter through six months
Design	Cochrane review
Study inclusion criteria	Controlled clinical trials and observational studies, published in all languages,. Studies of (or including) low birthweight (less than 2500 g) infants were included, provided that such infants were born at term (at least 37 completed weeks). Only those studies with an internal comparison group were included
Study exclusion criteria	Studies of preterm infants Studies based on external comparisons (with reference data) Studies comparing EBF and MBF from birth Studies that investigated the effects of age at introduction of nonbreast milk liquid or solid foods but did not ensure EBF at least three months prior to their introduction
Data collection	All data for our outcomes are from one or two of three cohort studies: Kramer 2000a (from PROBIT); Oddy (1999, Australia) and Duncan (1993, US)
Setting	Results for developing and developed countries presented separately
Case/ outcome definition (N) (inclusion/ exclusion)	The comparisons had to be based on one group of infants who were exclusively breastfed for at least six months, and-
Controls Definition (N) (inclusion/ exclusion, matching)	-another group of infants who received EBF for at least three but less than seven months and mixed breastfeeding (MBF) until six months or later (i.e., infants were introduced to liquid or solid foods between three and six months of age)
Exposure	EBF for at least 6 months vs EBF for at least 3 but less than 7 months with introduction to liquid or solid foods between 3 and 6 months
Measure of effect (if none, why?)	RR, 95% CI
Adjustment for confounders	The EBF group had a significantly reduced risk of one or more episodes of gastrointestinal infection in the first 12 months of life (RR 0.67; 95% CI 0.46 to 0.97) (outcome 47 Kramer 2000a), which was maintained in a multivariate mixed model controlling for geographic origin, urban versus rural location, maternal education, and number of siblings in the household (adjusted OR 0.61; 95% CI 0.41 to 0.93). The combined crude results of Oddy 1999 and Kramer 2000a show a substantial and statistically significant reduction in risk for hospitalization for respiratory tract

	infection (pooled RR 0.75; 95% CI 0.60 to 0.94), but the crude risk reduction in Kramer 2000a was nearly abolished and became statistically nonsignificant in a multivariate mixed model controlling for geographic region, urban versus rural location, maternal education and cigarette smoking, and number of siblings in the household (adjusted OR 0.96; 95% CI 0.71 to 1.30) (outcome 54).
Outcome, Significance	Gastrointestinal infection The EBF had a significantly reduced risk of one or more episodes of gastrointestinal infection in the first 12 months of life (RR 0.67; 95% CI 0.46 to 0.97) (outcome 47 Kramer 2000a), which was maintained in a multivariate mixed model controlling for geographic origin, urban versus rural location, maternal education, and number of siblings in the household (adjusted OR 0.61; 95% CI 0.41 to 0.93). No significant reduction in risk was observed for hospitalization for gastrointestinal infection, however (RR 0.79; 95% CI 0.42 to 1.49) (outcome 48 Kramer 2000a). Respiratory tract infection (upper, lower, hospitalisation) Oddy 1999 found no significant reduction of risk for one or more episodes of upper respiratory tract infection (outcome 49) in the EBF group (RR 1.07; 95% CI 0.96 to 1.20). Neither Oddy 1999 nor Kramer 2000a found a significantly reduced risk of two or more such episodes (pooled RR 0.91; 95% CI 0.82 to 1.02) (outcome 50). Nor did Oddy 1999 find a significant reduction in risk of four or more episodes of upper respiratory infection (RR 0.82; 95% CI 0.52 to 1.29) (outcome 51) or of one or more episodes of lower respiratory tract infection (RR 1.07; 95% CI 0.86 to 1.33) (outcome 52). Kramer 2000a found a small and nonsignificant reduction in risk of two or more respiratory tract infections (upper and lower combined) (RR 0.90; 95%CI 0.79 to 1.03) (outcome 53). The combined crude results of Oddy 1999 and Kramer 2000a show a substantial and statistically significant reduction in risk for hospitalization for respiratory tract infection (pooled RR 0.75; 95% CI 0.60 to 0.94), but the crude risk reduction in Kramer 2000a was nearly abolished and became statistically nonsignificant in a multivariate mixed model controlling for geographic region, urban versus rural location, maternal education and cigarette smoking, and number of siblings in the household (adjusted OR 0.96; 95% CI 0.71 to 1.30) (outcome 54).
Author's conclusion	Infants who are exclusively breastfed for six months experience less morbidity from gastrointestinal infection than those who are mixed breastfed as of three or four months. The available evidence demonstrates no apparent risks in recommending, as a general policy, exclusive breastfeeding for the first six months of life in both developing and developed-country settings.
Comment	Other outcomes are reported. Edited (no change to conclusions), published in Issue 1, 2009. Review content assessed as up-to-date: 29 December 2006

12) Respiratory tract infection as child outcome of not breastfeeding: corroborative study (repeats Bachrach 2003, see # 13 below)

Otitis media as child outcome of not breastfeeding: primary source of data

Necrotising enterocolitis (NEC) as outcome of not breastfeeding for babies in intensive (NICU) or special care baby units (SCBU): corroborative study

Ip S, Chung M, Raman G, Chew P, Magula N, DeVine D, Trikalinos T, Lau J. Breastfeeding and Maternal and Infant Health Outcomes in Developed Countries. Evidence Report/Technology Assessment No. 153 (Prepared by Tufts-New England Medical Center Evidence-based Practice Center, under Contract No. 290-02-0022). AHRQ Publication No. 07-E007. Rockville, MD: Agency for Healthcare Research and Quality. April 2007. AND **Ip et al (2009)** A Summary of the Agency for Healthcare Research and Quality's Evidence Report on Breastfeeding in Developed Countries. BREASTFEEDING MEDICINE Volume 4, Supplement 1, 2009. Mary Ann Liebert, Inc. DOI: 10.1089=bfm.2009.0050	
Objective	To review the evidence on the effects of breastfeeding on short- and long-term infant and maternal health outcomes in developed countries
Design	Systematic review
Study inclusion criteria	Systematic reviews/meta-analyses, randomized and nonrandomized comparative trials, prospective cohort and case-control studies on the effects of breastfeeding and relevant outcomes published in English. Included studies had to have a comparative arm of formula feeding or different durations of breastfeeding.
Study exclusion criteria	Studies were appraised for methodological quality. Only those with rigorous criteria for study selection, unbiased data collection, and appropriate methods of analyses were included.
Data collection	Searches of Medline, CINAHL, and the Cochrane Database of Systemic Reviews November 2005. Search terms included subject headings and text words relevant to breastfeeding and the different outcomes. Supplemental searches on selected outcomes were conducted through May 2006. Other relevant studies were identified by technical experts or in bibliographies of selected reviews.
Setting	Developed countries
Case/ outcome definition (N) (inclusion/ exclusion)	• Acute otitis media: definitions varied – mostly based on clinical and otoscopic findings. • Lower respiratory tract infection: as Bachrach 2003 • Necrotising enterocolitis (NEC): Confirmed cases of NEC as provided by study authors (either pneumatosis intestinalis or confirmed at surgery)
Controls Definition (N)	• Acute otitis media: n/a • Lower respiratory tract infection: as Bachrach 2003 • Necrotising enterocolitis (NEC): n/a
Exposure	• Acute otitis media: any definition of breastfeeding duration compared with exclusive formula feeding • Lower respiratory tract infection: as Bachrach 2003 • Necrotising enterocolitis (NEC): there were four included studies. Three compared any human donor milk with exclusive formula, and the fourth

Measure of effect	• Acute otitis media: Odds Ratio (OR) with 95% confidence intervals (CI) • Lower respiratory tract infection: as Bachrach 2003 • Necrotising enterocolitis (NEC): Risk ratios (RR) with 95% CIs
Adjustment for confounders	• Acute otitis media: confounders commonly considered were parental history of allergy, number of siblings, use of day care, maternal smoking, gender, ethnicity and socioeconomic status • Lower respiratory tract infection: as Bachrach 2003 • Necrotising enterocolitis (NEC): n/a (study design). Authors note potential confounders include birthweight, ethnicity and sex
Outcome, Significance	• Acute otitis media (AOM) (term infants): • Pooled data from five cohort studies of good and moderate methodological quality showed an adjusted odds ratio of AOM of 0.60 (95%CI 0.46-0.78) comparing breastfeeding to exclusive bottle-feeding. Pooled adjusted odds ratio of AOM was 0.77 (95%CI 0.64- 0.91), when comparing children who were ever breastfed with children who were exclusively bottle-fed in two studies. The pooled adjusted odds ratio was 0.50 (95%CI 0.36-0.70), when comparing children who were exclusively breastfed for at least 3 or 6 months with those who were exclusively bottle-fed for at least 3 or 6 months in three studies. • Lower respiratory tract infections (LRTI) (term infants): as Bachrach 2003 • Necrotising enterocolitis (NEC): Meta-analysis of four RCTs with a total of 476 infants provided RR 4.42 (95% CI 0.18 to 0.96) for the development of NEC, in favour of breast milk
Author's conclusion	A history of breastfeeding is associated with a reduced risk of many diseases in infants and mothers. Future research would benefit from clearer selection criteria, definitions of breastfeeding exposure, and adjustment for potential confounders. Matched designs such as sibling analysis may provide a method to control for hereditary and household factors that are important in certain outcomes.
Comment	Key review Other outcomes examined in this review include (list from Ip et al 2009): Child outcomes - nonspecific gastroenteritis, atopic dermatitis, asthma (young children), obesity, type 1 and 2 diabetes, childhood leukemia, sudden infant death syndrome, cognitive performance, cardiovascular diseases and infant mortality; Maternal outcomes - type 2 diabetes, breast cancer, ovarian cancer, postpartum depression, osteoporosis return-to-prepregnancy weight, postpartum weight loss.

13) Respiratory tract infection as child outcome of not breastfeeding: corroborative study

Bachrach et al (2003) Breastfeeding and the Risk of Hospitalization for Respiratory Disease in Infancy: A Meta-analysis. Arch Pediatr Adolesc Med. 2003;157:237-243	
Objective	To examine breastfeeding and the risk of hospitalization for lower respiratory tract disease (LRTD) in healthy full-term infants with access to modern medical care
Design	Systematic review with meta-analysis
Study inclusion criteria	Participants: healthy full-term infants whose living conditions reflected those of affluent developed nations
Study exclusion criteria	Studies of sick, premature, and/or low birth weight infants ("sick newborns"), and children with recognized chronic illnesses (eg, cystic fibrosis), were excluded, except for studies of children with allergic conditions Studies that did not provide data for duration of exclusive breastfeeding for 2, 4, or 6 months or total (any) breastfeeding for longer durations were excluded
Data collection	Search included contacting authors
Setting	Industrialized nations only. Studies were ineligible if they focused on geographic regions where gross malnutrition is prevalent.
Case/ outcome definition (N) (inclusion/ exclusion)	LRTD was defined to include bronchiolitis, asthma, bronchitis, pneumonia, empyema, and infections due to specific agents (e.g. respiratory syncytial virus)
Controls Definition (N)	n/a - the seven studies in the meta-analysis used cohort designs
Exposure	Exclusive breastfeeding for 2, 4, or 6 months or total (any) breastfeeding for longer durations, versus no breastmilk/breastfeeding
Measure of effect	Relative risk (RR) and 95% confidence interval (CI). Number needed to treat to prevent one LRTD hospitalization by exclusive breastfeeding.
Adjustment for confounders	The effect remained stable and statistically significant after adjusting for the effects of smoking or socioeconomic status
Outcome, Significance	The outcome was LRTD hospitalization rates. Seven cohort studies comparing four or more months of exclusive breastfeeding with no breastfeeding were pooled using a random-effects model. Summary RR 0.28 (95% CI 0.14 to 0.54). The number of infants who would need to be breastfed exclusively for 4 or more months to prevent one LRTD hospitalization was 26.
Author's conclusion	Among generally healthy infants in developed nations, more than a tripling in severe respiratory tract illnesses resulting in hospitalizations was noted for infants who were not breastfed compared with those who were exclusively breastfed for 4 months
Comment	Two other reviews use the same study data as Bachrach et al 2003: • Ip et al (2007/9) – updated Bachrach et al's search, did not find any more studies and restated the findings of Bachrach et al (see #12 above). • McNeil et al (2010) What are the Risks Associated with Formula Feeding? A Re-Analysis and Review. BIRTH 37:1 March 2010 . This is a re-analysis of Ip et al and uses the same study data as both Ip et al and Bachrach et al.

14) Necrotising enterocolitis (NEC) as outcome of not breastfeeding for babies in intensive (NICU) or special care baby units (SCBU): primary source of data

Henderson et al (2009) Enteral feeding regimens and necrotising enterocolitis in preterm infants: multi-centre case-control study. ADC-FNN Online First, published on September 3, 2007 as 10.1136/adc.2007.119560	
Objective	To examine associations between various enteral feeding practices and the development NEC in preterm infants
Design	Multi-centre case-control study
Data collection	Parental consent to obtain details of the clinical history was obtained and antenatal, perinatal and postnatal clinical risk factors and feeding data were extracted and compared between the groups
Setting	Ten neonatal units in the north of Britain between January 2004 and December 2005
Case/ outcome definition (N) (inclusion/ exclusion)	Cases were preterm infants (<37 completed weeks' gestation) with NEC diagnosed using modified Bell criteria or at laparotomy or autopsy examination (n=53)
Controls Definition (N) (inclusion/ exclusion, matching)	When a case was reported, a participating neonatal centre was randomly selected and a control infant who had not developed NEC identified. Controls were more than 34 weeks' postmenstrual age at recruitment and therefore very unlikely to develop NEC subsequently. Cases and controls were frequency-matched for gestational age at birth in one of three bands (<28 weeks, 28-32 weeks, >32 weeks).
Exposure	Received breast milk, vs. had not received breast milk
Measure of effect	For our primary outcome: Odds ratio, 95% confidence interval
Adjustment for confounders	No significant differences were found between the cases and controls for antenatal, perinatal and postnatal risk factors considered. The only difference reported was had/ had not received breast milk
Outcome, Significance	Significantly fewer cases (infants with NEC) than controls (matched infants in the same unit without NEC) had received human breast milk [75% versus 91%: odds ratio= 0.32 (95% confidence interval (CI) 0.11 to 0.98)] (other outcomes are reported)
Author's conclusion	We found that feeding with human breast milk was associated with lower risk of NEC. These findings endorse the current practice of encouraging mothers to express breast milk for their preterm infants, and of supporting them to do so with evidence-based interventions.
Comment	Other outcomes are reported

15) Necrotising enterocolitis (NEC) as outcome of not breastfeeding for babies in intensive (NICU) or special care baby units (SCBU): corroborative study

McGuire W and Anthony MY. Donor human milk versus formula for preventing necrotising enterocolitis in preterm infants: systematic review. *Arch Dis Child Fetal Neonatal Ed* 2003 88: F11-F14	
Objective	To determine if enteral feeding with donor human milk compared with formula milk reduces the incidence of necrotising enterocolitis (NEC) in preterm or low birthweight infants
Design	Systematic review and meta-analysis of randomised controlled trials
Study inclusion criteria	Randomised and quasi-randomised controlled trials Studies included if parenteral nutrition was available during advancement of enteral feeds and groups received similar treatment other than type of milk feed
Study exclusion criteria	Studies excluded if the allocated milk feed was a supplement to the mother's expressed breast milk, not the infant's entire enteral intake
Data collection	From four small trials published 1982-1990, using Cochrane Neonatal Group methods for screening, data extraction and quality appraisal
Setting and participants	Preterm (<37 weeks gestation) or low birthweight (<2.5 k) infants in neonatal units
Case/ outcome definition (N) (inclusion/ exclusion)	• NEC as defined in trials • Confirmed NEC, radiological confirmation showing gas in the portal venous system or free air in the abdomen, or when NEC is confirmed at surgery or autopsy
Controls Definition (N)	n/a
Exposure	Donor human milk versus formula milk
Measure of effect	Relative risk (RR) and 95% confidence intervals (CI)
Adjustment for confounders	n/a
Outcome, Significance	None of the trials individually found any statistically significant difference in the incidence of NEC. However, meta-analysis found that feeding with donor human milk was associated with a significantly reduced relative risk (RR) of NEC. Infants who received donor human milk were three times less likely to develop NEC (RR 0.34; 95% confidence interval (CI) 0.12 to 0.99), and four times less likely to have confirmed NEC (RR 0.25; 95% CI 0.06 to 0.98) than infants who received formula milk
Author's conclusion	• Clinical applicability unclear due to age of trials • Larger trials could compare infant growth, development and incidence of adverse outcomes, including NEC
Comment	Three of the four studies included in this review are also included in Quigley et al 2007, who excluded the fourth[1] because "most infants in the breast milk group received their own mother's expressed milk rather than donor breast milk". [1]Sveningsen NW, Lindroth M, Lindquist B. A comparative study of varying protein intake in low birth weight infant feeding. Acta Paediatr Scand Suppl 1982;296:28-31.

16) Necrotising enterocolitis (NEC) as outcome of not breastfeeding for babies in intensive (NICU) or special care baby units (SCBU): corroborative study

Quigley M, Henderson G, Anthony MY, McGuire W. Formula milk versus donor breast milk for feeding preterm or low birth weight infants. *Cochrane Database of Systematic Reviews* 2007, Issue 4. Art. No.: CD002971. DOI: 10.1002/14651858.CD002971.pub2	
Objective	To determine the effect of formula milk compared with donor human breast milk on growth and development in preterm or low birth weight infants
Design	Cochrane systematic review of randomised controlled trials Primary outcomes growth & development, including cognitive outcomes Secondary outcomes 1. Death in the neonatal period (up to 28 days) and death prior to hospital discharge. 2. Necrotising enterocolitis confirmed by at least two features (listed) 3. Time after birth to establish full enteral feeding 4. Feeding intolerance (defined) 5. Incidence of invasive infection as determined by listed criteria
Study inclusion criteria	Participants: preterm (less than 37 weeks' gestation) or low birth weight (less than 2.5 kilograms) infants Design: controlled trials utilizing either random or quasi-random patient allocation
Study exclusion criteria	One study, Svenningsen 1982, was excluded because although 48 low birth weight infants were randomly assigned to formula milk versus breast milk, most infants in the breast milk group received their own mother's expressed milk rather than donor breast milk.
Data collection	Cochrane Neonatal Group methods
Setting	Resource-rich countries: included studies were set in UK N=3), US (n=3), Finland (n=1) and Hungary (n=1)
Case & Control definitions	n/a (SR of RCTs)
Exposure	Enteral feeding with formula milk versus donor breast milk. The allocated milk feed may form the entire enteral intake or be a supplement to maternal breast milk. Trials in which parenteral nutritional support is available during the period of advancement of enteral feeds are acceptable provided that the groups receive similar treatment other than the type of milk feed
Measure of effect (if none, why?)	RR, 95% CI
Adjustment for confounders	n/a (SR of RCTs)
Outcome, Significance	There was no evidence of an effect on neurodevelopmental outcomes. Meta-analysis of data from five trials demonstrated a statistically significantly higher incidence of necrotising enterocolitis in the formula fed group: typical relative risk 2.5 (95% confidence interval 1.2, 5.1); typical risk difference: 0.03 (95% confidence interval 0.01, 0.06; number needed to harm: 33 (95% confidence interval 17, 100).

	Invasive infection (Outcome 01.23): Reported by one trial only, which did not find a statistically significant difference in the incidence of invasive infection
Author's conclusion	In preterm and low birth weight infants, feeding with formula milk compared with donor breast milk results in a higher rate of short-term growth but also a higher risk of developing necrotising enterocolitis. There are only limited data on the comparison of feeding with formula milk versus nutrient-fortified donor breast milk. This limits the applicability of the findings as nutrient fortification of breast milk is now a common practice in neonatal care. Future trials may compare growth, development and adverse outcomes in infants who receive formula milk versus nutrient-fortified donor breast milk given as a supplement to maternal expressed breast milk or as a sole diet.
Comment	

17) Necrotising enterocolitis (NEC) as outcome of not breastfeeding for babies in intensive (NICU) or special care baby units (SCBU): corroborative study

Lucas A & Cold TJ (1990) Breast milk and neonatal necrotising enterocolitis. Lancet 1990; 336: 1519-23	
Objective	To explore the relation between early diet or feeding practice and the frequency of necrotising enterocolitis
Design	Prospective multicentre randomised controlled trial
Data collection	Not described in this paper
Participants and setting	Infants with birthweight <1850g, in five British neonatal units
Intervention, Control	Study A (three centres): Randomised to receive pasteurised banked donated breast milk vs. a nutrient-enriched preterm formula Study B (two centres): Randomised to receive standard term formula vs. the same nutrient-enriched preterm formula as in Study A. In both Study A and Study B, randomisation was stratified according to whether the mother provided breastmilk for her own infant.
Outcome	Necrotising enterocolitis, using the British Association for Perinatal Pediatrics classification based on features of the disease in 165 cases in 54 British centres (BMJ 1983; 287:824-6)
Measure of effect	Odds ratios (OR) and 95% confidence intervals (CI).
Adjustment for confounders	For non-randomised comparisons, logistic regression adjusted for length of gestation, birthweight, sex, birth asphyxia, previous blood transfusions, use of theophylline and frusemide, polycythaemia, respiratory disease, duration of umbilical artery catheterisation, age at first enteral feed, rate of incrementation of early feed volumes, maternal steroid treatment and centre effects. Independent variables in the logistic regression models were those factors above found to be significantly related to occurrence of necrotising enterocolitis.
Outcome, Significance	The only outcome from a randomised comparison of human milk vs. formula was three cases (one confirmed) of necrotising enterocolitis among 86 infants exclusively fed with donor milk vs. six cases (four confirmed) among 76 infants exclusively fed with preterm formula (OR 2.4 [95% CI 0.6 to 9.8] for all cases and OR 4.7 [95% CI 0.5 to 4.3] for confirmed cases). Authors note “the sample size was not large enough to detect a difference smaller than ten-fold in frequency of necrotising enterocolitis between these groups with adequate power.” Type of diet was the factor most strongly related to necrotising enterocolitis. For all cases of necrotising enterocolitis, a high haemoglobin concentration and respiratory distress were also significant factors.
Author’s conclusion	“With the fall in the use of breast milk in British neonatal units, exclusive formula feeding could account for an estimated 500 extra cases of necrotising enterocolitis each year. About 100 of these infants would die.”
Comment	This study is included in the SR by Quigley et al 2007

18) Obesity as baby/child outcome of not breastfeeding: primary source of data

Horta et al. Evidence on the long-term effects of breastfeeding : systematic review and meta-analyses. WHO 2007.	
Objective	To assess the effects of breastfeeding on blood pressure, diabetes and related indicators, serum cholesterol, overweight and obesity, and intellectual performance
Design	Systematic review and meta-analyses
Study inclusion criteria	Observational and randomized studies, published in English, French, Portuguese and Spanish, assessing the effects of breastfeeding on blood pressure, obesity/overweight, total cholesterol, type-2 diabetes, and intellectual performance
Study exclusion criteria	Studies that restricted the measurement of outcomes to infancy were excluded from the meta-analyses
Data collection	Two reviewers independently evaluated study quality, using a standardized protocol, and disagreement was resolved by consensus rating
Setting	There was a sub-group analysis by study setting (high-income country vs. Middle/low income country)
Case/ outcome definition (N) (inclusion/ exclusion)	Different studies used different criteria and percentiles to define obesity. "Results of the studies have been similar. Arenz et al (*107*) reported no difference in mean effect among studies using the 90th, 95th or 97th percentile to define obesity. Therefore, differences in the definition of overweight/obesity should not be considered as a major methodological flaw in this meta-analysis. Existing cut-offs for overweight/obesity will have to be reassessed in the light of the new WHO Growth Standards" (Horta 2007 page 25)
Controls Definition (N)	Different studies used different criteria
Exposure	The type of comparison group used (e.g. never breastfed or breastfed for less than *x* months) did not constitute a selection criterion. The studies were heterogeneous. Table 3.1 (pp 28-30 of report) shows a comparison between: • any amount of breastfeeding (including exclusive, in 3/39 estimates) for any length of time, vs. • any lesser amount or time of breastfeeding (including never breastfed, in 23/39 estimates)
Measure of effect	OR (95% CI)
Adjustment for confounders	In these random-effects regression (meta-regression) models, each of the items used to assess study quality was considered as a covariate. Furthermore, the following study characteristics were also included as covariates in random-effects regression: a) Definition of breastfeeding b) Birth year c) Age at outcome assessment: (0) 1–9 yrs, (1) 10–19 yrs, (2) >19 yrs d) Study size (n) e) Provenance (high-income country /middle/low-income country).
Outcome, Significance	The outcome was risk of being considered as overweight/ obese. "We obtained 39 estimates of the effect of breastfeeding on prevalence of overweight/obesity. In a random-effects model, breastfed individuals were less likely to be considered as overweight and/or obese, with a pooled odds ratio of 0.78 (95% CI: 0.72–0.84).

	Control for confounding, age at assessment, year of birth, and study design did not modify the effect of breastfeeding. Because a statistically significant protective effect was observed among those studies that controlled for socioeconomic status and parental anthropometry, as well as with >1500 participants, the effect of breastfeeding was not likely to be due to publication bias or confounding."
Author's conclusion	The evidence suggests that breastfeeding may have a small protective effect on the prevalence of obesity. The effect seems to be more important against obesity than against overweight. Because the great majority of the published studies were conducted in Western Europe and North America, we are not able to assess whether this association is present in low and middle-income settings.
Comment	For our review we wanted studies adjusted for socioeconomic status and parental anthropometry that were undertaken in high income countries. Horta et al 2007 reported adjustment and setting as two separate subgroups: a) a pooled odds ratio (0.77 [0.71 to 0.83]) derived from 33 outcomes of a number of studies that were undertaken in high income countries ("the great majority of the published studies were conducted in Western Europe and North America", p. 33), regardless of how confounding was controlled for b) a pooled odds ratio (0.77 [0.71 to 0.84]) derived from 20 outcomes of a number of studies that adjusted for socioeconomic status and parental anthropometry, regardless of country income of the study setting. Two reviewers (FM and MJR) checked the forest plot, Fig 3.3. None of the 39 ORs is a true outlier. 5/39 are in the "favours not breastfeeding" section. Of these, two were undertaken in high income countries (Dubois 2005, Reilly 2005). The other three were undertaken in middle/low income countries. MJR, MQ and FM therefore concluded we are safe to use the pooled odds ratio b) above as the ORs do not appear to differ by country income.

19) Obesity as baby/child outcome of not breastfeeding: corroborative study

Study ref: Julie Armstrong, John J Reilly, and the Child Health Information Team. Breastfeeding and lowering the risk of childhood obesity. THE LANCET • Vol 359 • June 8, 2002	
Objective	To test the hypothesis that breastfeeding is associated with a reduced risk of obesity in a population-based sample
Design	Cohort of Scottish children born in 1995 or 1996
Data collection	At routine Child Health Surveillance Programme reviews a) by health visitor at infant age 6–8 weeks and b) at child age 39–42 months of age.
Setting	Scotland
Case/ outcome definition (N) (inclusion/ exclusion)	Scottish children studied at age 39–42 months in 1998 and 1999 (n=32, 200 with complete records, 62% of the original sample) Obesity was defined as body-mass index (BMI) at the 95th and 98th percentiles or higher.
Controls Definition (N) (inclusion/ exclusion, matching)	n/a
Exposure	Feeding data from Health Visitor records at infant age 6-8 weeks were Breastfed, fed on formula, or both. Comparison was any breastfeeding vs. Formula feeding.
Measure of effect	OR (95% CI)
Adjustment for confounders	The prevalence of obesity was significantly lower in breastfed children, and the association persisted after adjustment for socioeconomic status, birthweight, and sex.
Outcome, Significance	The adjusted odds ratio for obesity (BMI ≥98th percentile) (with any breastfeeding vs formula feeding) was 0·70 (95% CI 0·61–0·80).
Author's conclusion	Our results suggest that breastfeeding is associated with a reduction in childhood obesity risk
Comment	

20) Obesity as baby/child outcome of not breastfeeding: corroborative study

Li et al. Breast feeding and obesity in childhood: cross sectional study. BMJ VOLUME 327 18 OCTOBER 2003	
Objective	To assess whether breast feeding influences body mass index and obesity in childhood
Design	We used data from a randomly selected sample (n = 2584) of the members of the 1958 British birth cohort who had children by 1991, relating to their offspring.
Data collection	Data used by Li et al had been collected in 1991 when children were aged 4-18 yrs, on duration of bf, body mass index of children and confounding factors.
Setting	Children of people born in Britain in 1958
Case/ outcome definition (N) (inclusion/ exclusion)	Body mass index was standardised relative to the 1990 British growth reference. Obesity was defined as a standard deviation score > 1.64 (95th centile).
Controls Definition (N) (inclusion/ exclusion, matching)	n/a
Exposure	The breastfeeding categories reported are: <1 week, 1 week to 1 month, 2-3 months, 4-6 months, 7-9 months, >9 months. The words “exclusive” and “formula” do not appear in the paper
Measure of effect	OR (95% CI)
Adjustment for confounders	We calculated odds ratios before and after adjusting for sex, parent’s body mass index, maternal smoking during pregnancy, birth weight, and social class.
Outcome, Significance	Mean body mass index and obesity were consistently lower in those breast fed for 2-3 months, though not significantly (table).We found no evidence that breast feeding influenced body mass index or obesity and no dose dependent trend in either age group; adjustment for confounding factors did not alter these findings.
Author’s conclusion	As in the 1958 birth cohort (Parsons et al 2003) results from their offspring provide no support for a protective effect of breast feeding on obesity
Comment	Poor definition of exposure. It is not clear whether or not the 1958 birth cohort reported “no breastfeeding” or “exclusive breastfeeding”

21) Obesity as baby/child outcome of not breastfeeding: corroborative study

Reilly et al. Early life risk factors for obesity in childhood: cohort study. BMJ, doi:10.1136/bmj.38470.670903.E0 (published 20 May 2005)	
Objective	To identify risk factors in early life (up to 3 years of age) for obesity in children in the United Kingdom.
Design	Prospective cohort study
Data collection	How infant feeding data were collected is not reported in this paper. ALSPAC methodology paper (Golding 2001) says there were 3 postal questionnaires to mothers during the first 6 months of life. It is likely the infant feeding data came from those questionnaires. This paper reports "We measured height to 0.1 cm using the Harpenden stadiometer (Holtain; Crymych, Wales). Weight was measured to 0.1 kg. From these values we calculated the body mass index."
Setting	Avon Longitudinal Study of Parents And Children, United Kingdom (ALSPAC)
Case/ outcome definition (N) (inclusion/ exclusion)	Obesity at age 7 years, defined as a body mass index ≥ 95th centile relative to reference data for the UK population in 1990. 8234 children in cohort aged 7 years
Controls Definition (N)	n/a
Exposure	Exclusive breastfeeding at 2 months; Stopped or non-exclusive breastfeeding at 2 months; Never breastfed
Measure of effect	OR (95% CI)
Adjustment for confounders	Multivariable analysis for the prevalence of obesity using 25 risk factors.
Outcome, Significance	The apparent protective effect of exclusive breastfeeding on obesity at age 7 observed in the univariable analysis remained when breastfeeding was considered together with the other infant feeding and weaning practice variable (adjusted odds ratio 0.70, 95% confidence interval 0.54 to 0.91), but had disappeared in the final model
Author's conclusion	Eight of 25 putative risk factors were associated with a risk of obesity in the final models. Breastfeeding was not one of these. The eight factors were: 1. parental obesity (both parents: adjusted odds ratio, 10.44, 95% confidence interval 5.11 to 21.32) 2. very early (by 43 months) body mass index or adiposity rebound (15.00, 5.32 to 42.30) 3. more than eight hours spent watching television per week at age 3 years (1.55, 1.13 to 2.12) 4. catch-up growth (2.60, 1.09 to 6.16) 5. standard deviation score for weight at age 8 months (3.13, 1.43 to 6.85) and 18 months (2.65, 1.25 to 5.59) 6. weight gain in first year (1.06, 1.02 to 1.10 per 100 g increase) 7. birth weight, per 100 g (1.05, 1.03 to 1.07); and 8. short (< 10.5 hours) sleep duration at age 3 years (1.45, 1.10 to 1.89).
Comment	

22) Obesity as baby/child outcome of not breastfeeding: corroborative study

Wilson et al (1998) Relation of infant diet to childhood health: seven year follow up of cohort of children in Dundee infant feeding study. BMJ Vol. 316 3 Jan 1998 FOLLOW UP TO: **Howie et al (1990)** Protective effect of breastfeeding against infection. BMJ, 6 Jan, vol 300, pp 11-16	
Objective	*Wilson et al (1998):* To investigate the relation of infant feeding practice to childhood respiratory illness, growth, body composition, and blood pressure *Howie et al (1990):*To assess the relations between breast feeding and infant illness in the first two years of life with particular reference to gastrointestinal disease (respiratory illness; ear, eye, mouth, and skin infections; infantile colic; eczema; and nappy rash are also reported).
Design	Prospective observational study of mothers and babies followed up for 24 months after birth (and at mean age 7.3 years by Wilson et al 1998)
Data collection	Women with singleton pregnancies recruited at 36 weeks' gestation at the antenatal clinic of one hospital in Dundee (September 1983 to May 1986) Infant feeding data from birth and at hospital discharge from hospital records Detailed observations of infant feeding and illness collected during home visits by health visitors on standardised forms at: two weeks; one, two, three, four, five, six, nine, 12, 15, 18, 21, and 24 months. *At mean age 7.3 years (Wilson et al)*, measurements of children's height, weight, skinfold thickness (at four sites), bioelectrical impedance (to calculate percentage body fat), and blood pressure.
Setting	Community setting in Dundee, Scotland
Case/ outcome definition (N) (inclusion/ exclusion)	Inclusion (n=674 in original cohort and n=412 with complete data at 7.3 years) Women in a stable relationship living in Dundee (n=750) recruited Sep 1983 to Dec1984; Mar-Aug 1985; and Dec 1985 to May 1986 Exclusion: Premature birth (<38 weeks), low birth weight (<2500 g), or infant in special care >48 hours *Wilson et al (1998) followed up 412/674 at mean age 7.3 years and found:* • no significant differences in birth weight, gestation, parity, or solid feeding group between data on children followed up and those not traced/ excluded from the analysis (exclusions were for missing data) • proportionally more of the children who were not followed up were in social class IV but proportionally fewer children had parents who were unemployed • differences in infant feeding group (significance not reported): overall 19% (n=129) of the original cohort were not available for respiratory analysis: 21% of the original bottle feeding group (n=55), 16% (n=39) of those partially breastfed, and 14% (n=23) of those exclusively breastfed
Controls	n/a
Exposure	Wilson et al 1998 report these three feeding groups: Exclusive bf ≥15 weeks - solids before or at/after 15 weeks Partial breastfeeding <15 weeks - solids before or at/after 15 weeks Bottle feeding - solids before or at/after 15 weeks Howie et al 1990 reported: At each scheduled visit by the health visitor details of the infant feeding in the 24 hours before the visit were recorded. On the basis of the infant

	feeding record mothers were allocated into one of four infant feeding groups 5. Full breast feeders: breastfed for ≥13 weeks, did not introduce supplements before 13 weeks (n=97) 6. Partial breast feeders: breastfed for ≥13 weeks, introduced supplements before 13 weeks (n=130) 7. Early weaners: started breastfeeding, discontinued before 13 weeks (n=180) 8. Bottle feeders: bottle fed from birth (never breastfed) (n=267)
Measure of effect	*Wilson et al (1998)* Mean weight standard deviation score, percentage body fat and mean body fat from impedance
Adjustment for confounders	*Wilson et al (1998)* Growth and body composition in childhood Height; maternal height, socioeconomic group, birth weight, and sex; weight, body mass index, and percentage body fat; sex, birth weight, and weight at first solids were related significantly to growth and body composition in childhood, and were adjusted for in the multiple regression analyses.
Outcome, Significance	*At mean age 7.3 years (Wilson et al 1998)* Body mass index and height were not significantly different between the milk feeding groups. Children who had been given solids before 15 weeks were significantly heavier than those given solids at 15 weeks or later (mean weight standard deviation score 0.02 (- 0.02 to 0.06) *v* - 0.09 (- 0.16 to 0.02)). The percentage of body fat measured either by skinfold thickness or impedance was significantly greater in the children who had been given solid foods before 15 weeks of age (mean body fat from impedance 18.5% (18.2% to 18.8%) *v* 16.5% (16.0% to 17.0%)). Body fat was also greater in girls than boys (P < 0.01). The data were also analysed using infant feeding as continuous variables. This produced similar results, with the percentage of body fat and weight being greater in the children who were introduced to solids earlier.
Author's conclusion	*Wilson et al (1998)* This study indicates that in an industrialised society exclusive breast feeding for at least 15 weeks and the avoidance of solid foods before 15 weeks in healthy term infants may confer significant longterm health benefits on the child. If the hypothesis of programming is correct, the observed differences in body composition and blood pressure may become magnified with time and be important antecedents of adult disease. These data provide clinical evidence to support the current national recommendations for breastfeeding and timing of introduction of solids.
Comment	

23) Sudden Infant Death (SIDS) as baby outcome of not breastfeeding: primary source of data

Hauck et al (2011) Breastfeeding and Reduced Risk of Sudden Infant Death Syndrome: A meta-analysis. Pediatrics; originally published online June 13, 2011 DOI: 10.1542/peds.2010-3000 ALSO **Hauck & Tanabe (2009)** Clinical evidence: SIDS. Clinical Evidence 2009;06:315	
Objective	To perform a meta-analysis to measure the association between breastfeeding and SIDS
Design	Meta-analysis of observational studies "This report of our methods and findings follows the reporting guidelines proposed by Stroup et al22 and the PRISMA Group"
Study inclusion criteria	To be included studies had to meet 6 criteria developed by the American Academy of Pediatrics Task Force on Positioning and SIDS for its literature review on the relationship between sleeping position and SIDS. These criteria are (1) an appropriate definition for SIDS (2) autopsies performed in >98% of cases (3) an adequate description of SIDS ascertainment in the study population (4) matched control subjects (5) an adequate description of the process of control selection (6) inclusion of sufficient data to calculate ORs and 95% CIs or inclusion of the actual ORs and CIs.
Study exclusion criteria	In our review, 19 of 24 studies satisfied all 6 criteria; the failed criteria of 5 studies are listed in Table 1. Another study could not be included because the ORs were presented in a way that was not compatible with our analyses, which resulted in a total of 18 studies for the meta-analysis.
Data collection	Two teams of 2 reviewers evaluated study quality – (the 2009 report may have more details of data collection – the methods look good)
Setting	There were no country or language restrictions for this review. Provided Tasmania counts as a developed/ transitional country, all the included studies meet our inclusion criteria.
Case/ outcome definition (N) (inclusion/ exclusion)	In this review (2009 clinical evidence paper) SIDS was defined as "the sudden death of an infant under 1 year of age that remains unexplained after review of the clinical history, examination of the scene of death, and post-mortem."
Controls Definition (N) (inclusion/ exclusion, matching)	The 2011 paper states (above 4 & 5) that studies had to have matched controls and had to provide an adequate description of the process of control selection. However, the process of control selection in the included studies is not reported in either paper (2009 or 2011).
Exposure	Several different definitions for breastfeeding were examined: 1) breastfeeding of any amount (partial or exclusive) or duration, including breastfeeding at discharge from hospital ("any breastfeeding") VS ?? 2) breastfeeding of any amount at the age of 2 months or older ("breastfeeding ≥2 months") VS ?? 3) exclusive breastfeeding (ie, no formula supplementation) for any duration ("exclusive breastfeeding") VS ??

Measure of effect	Univariable and multivariable odds ratios were extracted. A summary odds ratio (SOR) was calculated for the odds ratios by using the fixed-effect and random-effect inverse-variance methods of metaanalysis. The Breslow-Day test for heterogeneity was performed.
Adjustment for confounders	"The 2005 American Academy of Pediatrics policy statement on SIDS did not endorse breastfeeding as a means to reduce the risk of SIDS because of the insufficient strength of evidence available at that time. Although there were several studies that had found a protective effect of breastfeeding, after controlling for possible confounding factors, the protective effect had been eliminated for some, so clear conclusions could not be drawn. Studies published since that statement, which are included in our current meta-analysis, notably the more detailed analysis of Vennemann et al, (Vennemann MM, Bajanowski T, Brinkmann B, et al; GeSID Study Group. Does breastfeeding reduce the risk of sudden infant death syndrome? *Pediatrics*. 2009;123(3)) showed a strongly protective effect of breastfeeding even after controlling for confounders. The meta-analysis by Ip et al consisted of many but not all of the studies included in our current analysis, and our findings were similar to theirs." (Vennemann et al 2009 (undertaken in Germany) state "in the multivariate analysis, we controlled for the following variables: • maternal smoking in pregnancy • maternal family status • maternal age at delivery • socioeconomic status of the family (socioeconomic status was calculated using school education, present work position, and income) • previous live births • birth weight of the infant • bed sharing in the last night • pillow in the infant's bed • additional heating during the last sleep (a hot water bottle in the infant's bed or the bed in front of a heater) • position placed to sleep • pacifier use during the last sleep")
Outcome, Significance	For infants who received any amount of breast milk for any duration, the univariable SOR was 0.40 (95% confidence interval [CI]: 0.35– 0.44), and the multivariable SOR was 0.55 (95% CI: 0.44–0.69). For any breastfeeding at 2months of age or older, the univariable SOR was 0.38 (95% CI: 0.27– 0.54). The univariable SOR for exclusive breastfeeding of any duration was 0.27 (95% CI: 0.24–0.31)
Author's conclusion	Breastfeeding is protective against SIDS, and this effect is stronger when breastfeeding is exclusive. The recommendation to breastfeed infants should be included with other SIDS risk-reduction messages to both reduce the risk of SIDS and promote breastfeeding for its many other infant and maternal health benefits.
Comment	

24) Cognitive outcomes in children who had been born at term, and in children who had been admitted to intensive (NICU) or special care baby units (SCBU), of not breastfeeding: primary source of data

Quigley MA, Hockley C, Carson C, Kelly Y, Renfrew MJ, Sacker A. Breastfeeding is Associated with Improved Child Cognitive Development: A Population-Based Cohort Study. The Journal of Pediatrics Vol. 160, Issue 1, January 2012, pp 25-32.	
Objective	To assess the association between breastfeeding and child cognitive development in term and preterm children
Design	Analysis of data from the United Kingdom Millennium Cohort Study, a nationally representative longitudinal study
Data collection	• A random two-stage sample of all infants born in England and Wales between September 2000 and August 2001, and in Scotland and Northern Ireland between November 2000 and January 2002, who were alive and living in the UK at age 9 months was drawn from Child Benefit registers. Children were recruited at approximately age 9 months (sweep 1), and detailed information was collected on a range of socio-economic and health factors by parental interview. Parents were interviewed again when the children were 3, 5 and 7 years (sweeps 2-4) • Breastfeeding initiation was assessed by the sweep 1 question "*Did you ever try to breastfeed your baby*?" Breastfeeding duration and exclusivity were estimated using the sweep 1 questions about the age of the infant when last given breast milk, and when first given formula, other types of milk and solids • Breastfeeding duration beyond sweep 1 was assessed using the sweep 2 question *"How old was the child when s/he last had breast milk"* • Cognitive development was assessed at age 5 years (sweep 3)
Setting	UK
Case/ outcome definition (N) (inclusion/ exclusion)	Definition (N): • Cognitive development was assessed using the Naming Vocabulary, Pattern Construction and Picture Similarities subscales of the British Ability Scales tests (BAS), administered at age 5 years • The study population was based on 11,879 children (11,101 who were born at term and 778 born preterm). The number of children with data on BAS subscales at sweep 3 was 11,705 for naming vocabulary, 11,720 for picture similarities and 11,658 for pattern construction (i.e. 79% of the eligible population who were recruited in sweep 1). Inclusion • White, singleton children with a gestational age at birth of at least 28 completed weeks, for whom the main respondent was the child's natural mother Exclusion • Children from non-white ethnic groups, because of concerns about the validity of the BAS assessments in these groups • Children who did not speak English at home • Children who were born extremely preterm (gestation <28 weeks), because they are more likely to have had complex feeding patterns and developmental problems which may not have been accurately captured in the MCS data
Controls	n/a
Exposure	• The duration of "any breastfeeding" (i.e. exclusive or partial breastfeeding) and "exclusive breastfeeding" were grouped into two-month bands: • never breastfed; <2.0 months; 2.0-3.9 months; ≥ 4.0 months

	• In the term group (but not in the preterm group), numbers were large enough to separate out those breastfed for ≥ 4 months as follows: • 4-5.9 months, 6.0-11.9 months, ≥ 12.0 months • No information was available about the types of formula fed to those who never breastfed or who supplemented breastfeeding
Measure of effect	A variable was considered statistically significant if any of its coefficients yielded a Wald test p-value <0.05. The coefficients from the fully adjusted regression models were expressed as the equivalent progress one would expect over a month in an average five year old; this was done using the age-equivalents derived for the MCS population[17-18]
Adjustment for confounders	First, adjustment was made for the following pregnancy-related and socio-demographic confounders: • Planned pregnancy • Mother's first-born child • Maternal alcohol and smoking in pregnancy • Whether the baby had special/intensive care at birth • Maternal age, marital status and education *(not maternal IQ)* • Social class • Whether languages other than English were spoken in the household Variables in this group were included in the models if they were significantly (p<0.05) associated with the outcome after adjustment for other socio-demographic and pregnancy-related variables in the model; this model is referred to as *partially adjusted*. Second, adjustment was made for the following potential mediators related to parenting and early years learning: • Mother's and father's parenting beliefs and time spent doing childcare activities as reported at sweep 1 • Condon maternal attachment questionnaire at sweep 1 • Frequency of mother and father doing activities (e.g. reading, drawing) with the child at sweep 3; • Mother's perceived parenting competence at sweep 3 • Maternal depression measured using the Malaise Inventory score at sweep 1 and Kessler questionnaire at sweep 3 • Child care at sweep 1 (none, nursery, child minder, informal) • Child's age in months when started formal child care • Number of months since child had started school and whether full-time or part-time Variables in this group were added to the *partially adjusted* models if they were significantly (p<0.05) associated with the outcome after adjustment for the other parenting and early years variables; these models are referred to as *fully adjusted*.

Outcome, Significance	The mean scores for all subscales increased with breastfeeding duration. After adjusting for confounders, there was a significant difference in mean score between those breastfed and those never breastfed: • in term children, a 2 point increase in score for picture similarities (if breastfed for ≥4 months) and naming vocabulary (if breastfed for ≥6 months) • in preterm children, a 4 point increase for naming vocabulary (if breastfed for ≥4 months) and picture similarities (if breastfed for ≥2 months) and a 6 point increase for pattern construction (if breastfed for ≥2 months) These differences suggest that breastfed children will be 1-6 months ahead of children who were never breastfed
Author's conclusion	In white, singleton UK children, breastfeeding, particularly when it is prolonged, is associated with improved cognitive development, particularly in those born preterm
Comment	

25) Cognitive outcomes in children who had been born at term, and in children who had been admitted to intensive (NICU) or special care baby units (SCBU), of not breastfeeding: corroborative study

Iacovou, M and Sevilla-Sanz, A. The Effect of Breastfeeding on Children's Cognitive Development. Institute for Social and Economic Research no. 2010-40, 13 December 2010	
Objective	To investigate the causal effect of breastfeeding on children's cognitive development
Design	Analysis of data from a longitudinal study, using Propensity Score Matching (PSM)
Data collection	Data from the Avon Longitudinal Study of Parents And Children (ALSPAC). Children born early 1990s. Test score data from local school entry tests and national SATS tests administered at the end of "Key stages" in schools.
Setting	UK (Bristol area)
Case/ outcome definition (N) (inclusion/ exclusion)	14, 472 ALSPAC core sample pregnancies with known birth outcome. 195 of these were twin pregnancies and were included in the dataset. Four pregnancies were triplet or quadruplet and these were excluded. Therefore 14, 472 mothers and 14, 667 infants in this data set. The number of infants "ever breastfed at 4 weeks" in the analysis is stated to be "approximately half"
Controls Definition (N) (inclusion/ exclusion, matching)	Propensity Score Matching used. Each breastfed baby was "twinned" (on "a huge range of characteristics" including infant sex, gestational age & birthweight; mothers' age & marital status; both parents' job status, education and attitudes to breastfeeding as measured before birth; characteristics of their home and neighbourhood) with one or more babies who were not breastfed, but who in all other observable respects are similar to the breastfed baby.
Exposure	Ever breastfed vs. never breastfed at 4 weeks *(additional information clarified with authors by FM)*
Measure of effect	Ordinary Least Squares (OLS) regressions, as a benchmark against which to compare PSM results.
Adjustment for confounders	Control variables are listed in appendix A under the headings Breastfeeding variables, Age at the time of the test, Socio-demographic variables at or during pregnancy, Pregnancy and delivery information and Parenting styles.
Outcome, Significance	OLS and PSM coefficients for test scores in reading, writing and maths at entry level (age 5) and Key Stages 1 (age 7), 2 (age 11) and 3 (age 14). "Controlling for a wide range of factors, children breastfed at four weeks or more do better than children breastfed for less than four weeks by about one tenth of a standard deviation (slightly less at younger ages and slightly more at older ones) The use of the PSM technique to control for heterogeneity suggests that these differences are likely to be causal"
Author's conclusion	The "raw" difference between children who were and were not breastfed at 4 weeks is large, at a little over one third of a standard deviation. Most of this difference may be explained by maternal characteristics. However, even after controlling for these, a statistically significant difference remains. This is smaller, however, it is statistically significant across English, maths and science scores, and it persists at least until age fourteen: indeed there is some evidence that the effect tends to grow over time.
Comment	Note "determinants of children´s cognitive outcomes not considered in our analysis include the mother's IQ"

Appendix 12: Economic Model Input Parameters

Gastroenteritis parameters

Parameters	Model input	Definition and unit	Data source:
Births and deaths		-	
Number of children born in 2009	790,938	2009 population multiplied by live birth rate of 12.8/1000.	ONS Population and vital rates: International (http://www.statistics.gov.uk/STATBASE/Product.asp?vlnk=15354)
Infant (up to 1 year) mortality	3,638	2009 infant mortality of 4.6 per 1000 live births	ONS Population and vital rates: International (http://www.statistics.gov.uk/STATBASE/Product.asp?vlnk=15354)
Neonatal (up to 28 days) mortality	2,452	2009 neonatal mortality rate per 1000 live births	ONS Child Mortality statistics (http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-213277)
Breastfeeding rates			
Current rate of exclusive breastfeeding (EBF) at 4 month	0.07	Observed exclusive breastfeeding at 4 months rate in the UK	Infant Feeding Survey 2005
Current rate of EBF at 6-week	0.21	EBF for 6 weeks	Infant Feeding Survey 2005
Current rate of EBF at 1-week	0.45	EBF for 1 week	Infant Feeding Survey 2005
Current rate of EBF at birth	0.65	EBF at birth	Infant Feeding Survey 2005
Current rate of EBF at 6-month	0.005	EBF at 6-month	Infant Feeding Survey 2005
Current **prevalence** (any breastfeeding) at 6 month	0.25	Partial breastfeeding at 6 month	Infant Feeding Survey 2005
Current **prevalence** (any breastfeeding) at 6 week	0.48	Partial breastfeeding at 6 week	Infant Feeding Survey 2005
Odds ratios			
OR {GP cases of GI infection; current BF; any}	0.36	Adjusted OR in favour for current infant feeding (breast milk and formula); 1993-96	Quigley et al. (2006)
OR {GP cases of GI infection; current BF; exclusive}	0.28	Adjusted OR in favour for current infant feeding (breast milk & solid - no formula); 1993-96	Quigley et al. (2006)

OR {hospitalisation; current BF; any}	0.52	Adjusted OR in favour for current partial BF in infants under 8 months; 2000-02	Quigley et al. (2007)
OR {hospitalisation; current BF; exclusive}	0.39	Adjusted OR in favour for current exclusive BF in infants under 8 months; 2000-02	Quigley et al. (2007)
Care episode incidences			
Incidence of hospital admissions - DH data	0.017	Admissions with GI in infants per live birth	Department of Health Infant Feeding Profiles (2011)
Incidence of primary care visits	0.047	GP consultations per child <1 year	RCGP 2010
Care episode Costs [inflated to 2009/10 prices]			
Average costs of hospitalisation	£ 806.52	£675 weighted average of routine and emergency admissions related to GI. 2003/04 prices	NICE 2006: Postnatal care guidance and cost reports
Reference (unit) cost of hospitalisation	£ 989.44	weighted average of Total HRG4 based on mapping from DH(2011) ICD codes (see 'hospital costs' tab)	Estimated by SP
Average costs of GP consultation	£ 36.00	Per surgery consultation lasting 11.7 minutes; 2009-10 prices	Curtis (2010)
Sensitivity analysis parameters			
Hospital admissions			
Lower limit of OR - hospitalisation; exclusive	0.18	Associated breastfeeding being more effective in reducing GI case	Quigley 2007
Upper limit of OR - hospitalisation; exclusive	0.85	Associated breastfeeding being less effective in reducing GI case	Quigley 2007
Lower limit of OR - hospitalisation; any	0.3	Associated breastfeeding being more effective in reducing GI case	Quigley 2007
Upper limit of OR - hospitalisation; any	0.87	Associated breastfeeding being less effective in reducing GI case	Quigley 2007
Lower quartile of unit cost of hospital admission	£ 585.63	Lower quartile unit cost estimated (see hospital costs tab)	NHS Reference Costs

Upper quartile of unit cost of hospital admission	£ 1,206.04	Upper quartile unit cost estimated (see hospital costs tab)	NHS Reference Costs
GP consultations			
Lower limit of OR - GP consultations; exclusive	0.11	Associated breastfeeding being more effective in reducing GI case	Quigley 2006
Upper limit of OR - GP consultations; exclusive	0.69	Associated breastfeeding being less effective in reducing GI case	Quigley 2006
Lower limit of OR - GP consultations; any	0.18	Associated breastfeeding being more effective in reducing GI case	Quigley 2006
Upper limit of OR - GP consultations; any	0.74	Associated breastfeeding being less effective in reducing GI case	Quigley 2006
Upper estimate - unit cost of GP consultation	£53	Higher end of GP consultation costs assuming 17.2 minutes of consultation time	Curtis et al. 2011

Lower respiratory tract infection (LRTI) parameters

Parameters	Model input	Definition and unit	Data source:
Births and deaths			
Number of children born in 2009	790,938	2009 population multiplied by live birth rate of 12.8/1000.	ONS Population and vital rates: International (http://www.statistics.gov.uk/STATBASE/Product.asp?vlnk=15354)
Infant (up to 1 year) mortality	3,638	2009 infant mortality of 4.6 per 1000 live births	ONS Population and vital rates: International (http://www.statistics.gov.uk/STATBASE/Product.asp?vlnk=15354)
Neonatal (up to 28 days) mortality	2,452	2009 neonatal mortality rate per 1000 live births	ONS Child Mortality statistics (http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-213277)
Breastfeeding rates			
Current rate of exclusive breastfeeding (EBF) at 4 month	0.07	Observed exclusive breastfeeding at 4 months rate in the UK	Infant Feeding Survey 2005
Current rate of EBF at 6-week	0.21	EBF for 6 weeks	Infant Feeding Survey 2005
Current rate of EBF at 1-week	0.45	EBF for 1 week	Infant Feeding Survey 2005
Current rate of EBF at birth	0.65	EBF at birth	Infant Feeding Survey 2005
Current rate of EBF at 6-month	0.005	EBF at 6-month	Infant Feeding Survey 2005
Current **prevalence** (any breastfeeding) at 6 month	0.25	Any breastfeeding at 6 month	Infant Feeding Survey 2005
Current **prevalence** (any breastfeeding) at 6 week	0.48	Any breastfeeding at 6 week	Infant Feeding Survey 2005
Hospitalisation odds ratio (mean)			
OR {hospitalisation; current BF; any}	0.67	Adjusted OR in favour for current partial BF in infants under 8 months; 2000-02; CI:(0.52-0.88)	Quigley et al. (2006)
OR {hospitalisation; current BF; exclusive}	0.7	Adjusted OR in favour for current infant feeding (exclusive breast milk); 2000-02. CI: (0.49-0.98)	Quigley et al. (2006)
Care episode incidence of LRTI			
Hospitalisation (LRTI defined over selected ICD codes)	0.0591	Per 1000 live births in England in 2009/10. Based on Hospital Episode Statistics	Department of Health (2011)

Primary care LRTI, defined by RCGP data	0.2343	23432.55846 per 100,000 population. Based on rcgp 2010 data on disease incidence	RCGP Annual Report (2010)
Care episode Costs [2009/10 prices]			
Average cost of hospitalisation (non-elective average of short, long, excess stay)	£1,078.42	Per admission. 2009-10 prices based on nhs reference costs	NHS Information Centre, HRG 2009-10
GP visits odds ratio (mean)			
OR {GP; current BF; any}	0.65	Adjusted OR in favour for any BF	Fisk et al. (2011)
OR {GP; current BF; exclusive}	0.69	Adjusted OR in favour for exclusive BF	Howie et al. (1990)
Sensitivity parameters			
Hospital admissions			
Lower limit of OR - hospitalisation; exclusive	0.49	Associated breastfeeding being more effective in reducing LRTI case	Quigley 2007
Upper limit of OR - hospitalisation; exclusive	0.98	Associated breastfeeding being less effective in reducing LRTI case	Quigley 2007
Lower limit of OR - hospitalisation; any	0.52	Associated breastfeeding being more effective in reducing LRTI case	Quigley 2007
Upper limit of OR - hospitalisation; any	0.88	Associated breastfeeding being less effective in reducing LRTI case	Quigley 2007
Lower quartile of unit cost of hospital admission	£749	Lower quartile unit cost estimated (see hospital costs tab)	NHS Reference Costs
Upper quartile of unit cost of hospital admission	£1,290	Upper quartile unit cost estimated (see hospital costs tab)	NHS Reference Costs
GP consultations			
Lower limit of OR - GP consultations; exclusive	0.47	Associated breastfeeding being more effective in reducing LRTI case	Howie (1990), estimated by MQ
Upper limit of OR - GP consultations; exclusive	1	Associated breastfeeding being less effective in reducing LRTI case	Howie (1990), estimated by MQ

Lower limit of OR - GP consultations; any	0.43	Associated breastfeeding being more effective in reducing LRTI case	Quigley 2006Fisk et al. (2011)
Upper limit of OR - GP consultations; any	0.96	Associated breastfeeding being less effective in reducing LRTI case	Quigley 2006Fisk et al. (2011)
Upper estimate - unit cost of GP consultation	£53	Higher end of GP consultation costs assuming 17.2 minutes of consultation time	Curtis et al. 2011

Acute Otitis Media (AOM) parameters

Parameters	Model input	Definition and unit	Data source:
Births and deaths			
Number of children born in 2009	790,938	2009 population multiplied by live birth rate of 12.8/1000.	ONS Population and vital rates: International (http://www.statistics.gov.uk/STATBASE/Product.asp?vlnk=15354)
Infant (up to 1 year) mortality	3,638	2009 infant mortality of 4.6 per 1000 live births	ONS Population and vital rates: International (http://www.statistics.gov.uk/STATBASE/Product.asp?vlnk=15354)
Neonatal (up to 28 days) mortality	2,452	2009 neonatal mortality rate per 1000 live births	ONS Child Mortality statistics (http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-213277)
Breastfeeding rates			
Current rate of exclusive breastfeeding (EBF) at 4 month	0.07	Observed exclusive breastfeeding at 4 months rate in the UK	Infant Feeding Survey 2005
Current rate of EBF at 6-week	0.21	EBF for 6 weeks	Infant Feeding Survey 2005
Current rate of EBF at 1-week	0.45	EBF for 1 week	Infant Feeding Survey 2005
Current rate of EBF at birth	0.65	EBF at birth	Infant Feeding Survey 2005
Current rate of EBF at 6-month	0.005	EBF at 6-month	Infant Feeding Survey 2005
Current **prevalence** (any breastfeeding) at 6 month	0.25	Any breastfeeding at 6 month	Infant Feeding Survey 2005
Current **prevalence** (any breastfeeding) at 6 week	0.48	Any breastfeeding at 6 week	Infant Feeding Survey 2005
Odds ratios in favour of breastfeeding			
OR {ear infection; BF; any}	0.4	Adjusted OR in favour for current partial BF in infants under 8 months; 2000-02; CI:(0.52-0.88)	Quigley et al. (2006)
OR {acute otitis media; BF; exclusive}	0.5	Adjusted OR in favour for current infant feeding (exclusive breast milk); 2000-02. CI: (0.49-0.98)	Quigley et al. (2006)
Care episode incidence of LRTI			Van Damme et al. (2007) JID article
Primary care (OM defined by 'Royal College of GP Database')	0.136	13556.08361 per 100,000 population, 2010	RCGP (2010)

Care episode Costs [2009/10 prices]			
Average cost of GP visits	£36.00	Per surgery consultation lasting 11.7 minutes; 2009-10 prices	Curtis (2010)
Sensitivity parameters			
GP consultations			
Lower limit of OR - GP consultations; exclusive	0.37	Associated breastfeeding being more effective in reducing LRTI case	Howie (1990), estimated by MQ
Upper limit of OR - GP consultations; exclusive	0.7	Associated breastfeeding being less effective in reducing LRTI case	Howie (1990), estimated by MQ
Lower limit of OR - GP consultations; any	0.21	Associated breastfeeding being more effective in reducing LRTI case	Quigley 2006Fisk et al. (2011)
Upper limit of OR - GP consultations; any	0.76	Associated breastfeeding being less effective in reducing LRTI case	Quigley 2006Fisk et al. (2011)
Upper estimate - unit cost of GP consultation	£53	Higher end of GP consultation costs assuming 17.2 minutes of consultation time	Curtis et al. 2011

Necrotising Enterocolitis (NEC) parameters

Parameters	Model input	Definition and unit	Data source:
Births and deaths			
Number of children born in 2009	790,938	2009 population multiplied by live birth rate of 12.8/1000.	ONS Population and vital rates: International (http://www.statistics.gov.uk/STATBASE/Product.asp?vlnk=15354)
Number of neonatal admissions	79,094	10% of all live births, estimated based on 2005 Neonatal Survey data	Neonatal Survey, NPEU Oxford
Breastfeeding rates			
Current rate of breastfeeding/ have breast milk (Policy D0)	0.35	35% of all reference population breastfed or have breast milk.	Bonet et al. (2009).
Hypothetical rate for Policy D1	0.50	50% of all reference population breastfed or have breast milk	Hypothetical
Hypothetical rate for Policy D2	0.75	75% of all reference population breastfed or have breast milk	Hypothetical
Hypothetical rate for Policy D3	1.00	100% of all reference population breastfed or have breast milk	Hypothetical
Odds ratios and relative risks in favour of breastfeeding			
RR in favour of breast milk	0.19	RR in favour for breastfeeding or receive breast milk (read comment)	Henderson et al. (2009)
Overall incidence of NEC			
Overall incidence - estimated based on HES observed data	0.01	Of all neonatal units admissions, estimated using HES England data (read comment)	Information Centre, Hospital Episode Statistics for England, 2009-10
Care episode Costs [2009/10 prices]			
Average cost of NEC surgery	£1,450.07	Per case in 2009/10 prices (read comment)	NHS Reference Costs 2009-10
Average bed-day cost in Neonatal Unit	£618.34	Per bed-day in neonatal units 2009/10 prices	NHS Reference Costs 2009-10
Mean length of stay in NEC cases	26.70	Days, observed in England	HES Online 2009-10

Distribution of NEC treatment			
Surgical	0.31	Of all NEC cases, estimated based on Rees et al. (2010)	Rees et al. (2010)
Medical	0.69	Of all NEC cases, estimated based on Rees et al. (2010)	Rees et al. (2010)
Costs parameters for sensitivity analysis			
Odds Ratio Lower 95% CI	0.05	Associated breastfeeding being more effective in reducing NEC case	Henderson et al. (2009)
Odds Ratio Upper 95% CI	0.73	Associated breastfeeding being less effective in reducing NEC case	Henderson et al. (2009)
Average bed day cost - lower quartile	£509.44	NHS Reference costs 2009-10 (see hospital costs tab)	NHS Reference costs 2009-10 (see hospital costs tab)
Average bed-day cost upper quartile	£712.17	NHS Reference costs 2009-10 (see hospital costs tab)	NHS Reference costs 2009-10 (see hospital costs tab)
Average cost of NEC surgery - lower quartile	£689.07	NHS Reference costs 2009-10 (see hospital costs tab)	NHS Reference costs 2009-10 (see hospital costs tab)
Average cost of NEC surgery - upper quartile	£1,802.20	NHS Reference costs 2009-10 (see hospital costs tab)	NHS Reference costs 2009-10 (see hospital costs tab)

Maternal breast cancer parameters

Parameters	Model input	Definition and unit	Data source:
Reference population			
Number of primiparous women	313,817	Estimated number of first mothers in the UK in 2009	ONS (2009) and EURO-PERISTAT Project (2008)
Mean age of women at first birth	28	Years. This is the average age of women in the UK who give birth for the first time	ONS (2009) Maternity and birth statistics
Average age of women at the onset of breast cancer	68	Years. This is the average age of all newly diagnosed breast cancer cases in the UK	Cancer Research UK (2009)
Breast cancer incidence and survival		-	
Lifetime risk of breast cancer - UK	0.125	Lifetime risk of 1 in 8 in the UK Population	Cancer Research UK (2009)
New cases of breast cancer per annum in the UK - average of 2006-2008	46,820	Total number of reported new cases in England and Wales, Scotland and Northern Ireland	Cancer Registry
Distribution of breast cancer new cases - average of 2006-2008			
15-49 years	0.1919	Percentage of total breast cancer cases	Cancer Research UK Statistics
50-69 years	0.4772	Percentage of total breast cancer cases	Cancer Research UK Statistics
70-99 years	0.3309	Percentage of total breast cancer cases	Cancer Research UK Statistics
20 year relative survival of breast cancer			
15-49 years	0.64	Percentage of total breast cancer cases relative to general population	Cancer Research UK Statistics
50-69 years	0.72	Percentage of total breast cancer cases relative to general population	Cancer Research UK Statistics
70-99 years	0.59	Percentage of total breast cancer cases relative to general population	Cancer Research UK Statistics

Overall mortality (annual probability of dying- all cause)			
15-49 years	0.0007	Life table mx values averaged across the age-group	ONS Life Table
50-69 years	0.0061	Life table mx values averaged across the age-group	ONS Life Table
70-99 years	0.1137	Life table mx values averaged across the age-group	ONS Life Table
Annual probability of dying among cancer patients			
15-49 years	0.0011	Estimated by applying relative survival on overall survival	
50-69 years	0.0085	Estimated by applying relative survival on overall survival	
70-99 years	0.1927	Estimated by applying relative survival on overall survival	
Breastfeeding rates			
Policy E0			
Never	0.32	Percentage of primiparous women breastfeeding	Liu et al (2009)
≤6 months	0.36	Percentage of primiparous women breastfeeding	Liu et al (2009)
7-18 months	0.16	Percentage of primiparous women breastfeeding	Liu et al (2009)
18+ months	0.16	Percentage of primiparous women breastfeeding	Liu et al (2009)
Policy E1			
Never	0.16	Percentage of primiparous women expected to breastfeed	Scenario created by Research Team
≤6 months	0.52	Percentage of primiparous women expected to breastfeed	Scenario created by Research Team
7-18 months	0.16	Percentage of primiparous women expected to breastfeed	Scenario created by Research Team

18+ months	0.16	Percentage of primiparous women expected to breastfeed	Scenario created by Research Team
Policy E2			
Never	0.16	Percentage of primiparous women expected to breastfeed	Scenario created by Research Team
≤6 months	0.36	Percentage of primiparous women expected to breastfeed	Scenario created by Research Team
7-18 months	0.32	Percentage of primiparous women expected to breastfeed	Scenario created by Research Team
18+ months	0.16	Percentage of primiparous women expected to breastfeed	Scenario created by Research Team
Policy E3			
Never	0.16	Percentage of primiparous women expected to breastfeed	Scenario created by Research Team
≤6 months	0.36	Percentage of primiparous women expected to breastfeed	Scenario created by Research Team
7-18 months	0.16	Percentage of primiparous women expected to breastfeed	Scenario created by Research Team
18+ months	0.32	Percentage of primiparous women expected to breastfeed	Scenario created by Research Team
Breast cancer relative risks			
Never breastfed	1		
BF for <6 months	0.98	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)
BF for 7-18 months	0.94	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)
BF for 19-30 months	0.89	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)
BF for 31-54 months	0.88	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)
BF for 55+ months	0.73	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)
BF for any duration	0.96	Relative risk in favour of breast feeding from a meta analysis	Estimated by Research Team based on figures provided in Beral et al. (2002)

BF for >18 months	0.89	Relative risk in favour of breast feeding from a meta analysis	Estimated by Research Team based on figures provided in Beral et al. (2002)
Care episode Costs (2009/10 prices)			
Average annual cost of breast cancer	£11,726	7, 247 per case. 1995/96 prices.	Dolan et al. (1999). The Breast 8, 205-207
Average annual cost of Stage IV breast cancer	£16,260	12500.76 per Stage IV case in 2002 prices	Remak & Brazil (2004). British Journal of Cancer 91, 77 – 83
Utility (baseline)	0.7117	Median of reported utilities across all stages of breast cancer	Derived from Table 38 of Robertson et al. (2011)
Utility (alternative)	0.8033	Median for highest severity	Derived from Table 38 of Robertson et al. (2011)
Utility (alternative)	0.5270	Mean across all severity	Derived from Table 38 of Robertson et al. (2011)
Utility (alternative)	0.6724	Median for lowest severity	Derived from Table 38 of Robertson et al. (2011)
Discount rate	0.035		
Discount rate (Baseline)	0.035	Rate applied to discount future stream of costs and qalys	NICE reference case
Discount rate (alternative)	0.000	Rate applied to discount future stream of costs and qalys	Alternative value in NICE Guidance to discount QALYs
Discount rate (alternative)	0.050	Rate applied to discount future stream of costs and qalys	Alternative value in DH Guidance to discount costs
Relative risks for sensitivity analysis	0.000		
Lower 95% CI value			
BF for <6 months	0.95	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)
BF for 7-18 months	0.91	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)
BF for 19-30 months	0.84	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)
BF for 31-54 months	0.82	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)
BF for 55+ months	0.63	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)

BF for any duration	0.92	Relative risk in favour of breast feeding from a meta analysis	Estimated by Research Team based on figures provided in Beral et al.
BF for >18 months	0.84	Relative risk in favour of breast feeding from a meta analysis	Estimated by Research Team based on figures provided in Beral et al.
Upper 95% CI value			
BF for <6 months	1.01	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)
BF for 7-18 months	0.97	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)
BF for 19-30 months	0.94	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)
BF for 31-54 months	0.94	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)
BF for 55+ months	0.83	Relative risk in favour of breast feeding from a meta analysis	Beral et al. (2002)
BF for any duration	0.99	Relative risk in favour of breast feeding from a meta analysis	Estimated by Research Team based on figures provided in Beral et al.
BF for >18 months	0.94	Relative risk in favour of breast feeding from a meta analysis	Estimated by Research Team based on figures provided in Beral et al.

Appendix 13
Sensitivity analyses

Economic analysis of gastrointestinal infection – sensitivity analyses

Deterministic sensitivity analyses assessed the impact on the estimated cost-savings of two key input parameters: the odds ratio for risk of hospitalisation for gastrointestinal infection (GI) and unit costs of treating GI. These parameters were selected to capture the changes in both outcomes (expected number of GI cases) and costs to treat those cases. The base case estimate was altered for a series of independent sensitivity analyses, in the following order:

- Change mean value of the odds ratio for risk of hospitalisation for GI to its lowest 95% confidence interval value
- Change mean value of the odds ratio for risk of hospitalisation for GI to its highest 95% confidence interval value
- Change national average unit cost of hospital admission for GI to lower quartile
- Change national average unit cost of hospital admission for GI to upper quartile
- Change unit cost of GP visit (based on 11.7 minutes) to unit cost of GP visit (based on 17.2 minutes)

Table 13.1, T**Error! Reference source not found.**able 13.2 and Figure 13.1 show the impact of the new estimates run in the sensitivity analyses relative to base case cost-savings. A positive % change (in Tables 3a and 3b) indicates higher cost-savings for a new estimate. In the sensitivity analysis of the ORs for risk of hospitalisation for different rates and definitions of breastfeeding, the same rates across the same type of policies (i.e. A1-A3) would be expected but different rates would be expected between scenarios (i.e. A vs. B or C). This is because the number of cases prevented by different policies will not be proportionate. However the % change figures for the sensitivity analysis of unit cost do not change because the total cost change is entirely influenced by the increment (+ or -) of unit cost.

The results of the sensitivity analysis on saved costs from hospitalisation (Table 3a) show that using the lower value of the odds ratio for risk of hospitalisation due to GI (which is associated with breastfeeding being more effective in reducing the number of GI cases) increases potential cost savings by 37%. Thus potential cost savings increase: from £1.2 million to £1.6 million per annum for policy A1; from £3.2 million to £4.4 million per annum for policy A2; and from £5 million to £6.7 million per annum for policy A3. Using the higher value of the odds ratio for risk of hospitalisation due to GI (which is associated with breastfeeding being less effective in reducing GI case) reduces potential cost savings by 76%. In this case the potential cost savings for policy A1 fall from £1.2 million to £280,000 per year and in the most optimistic scenario (policy A3) potential cost savings fall from £5 million to £1.2 million per year. Using the lower quartile of hospital costs reduces all potential hospital cost savings by 40% and using the higher quartile increases all potential hospital cost savings by 20%.

Using the lower value of the odds ratio for risk of GP consultation due to GI (which is associated with breastfeeding being more effective in reducing GI case) increases potential cost savings by 25%. Thus potential cost savings in primary care increase: from £140,000 to

£180,000 per annum for policy A1; from £380,000 to £480,000 per annum for policy A2; and from £580,000 to £730,000 per annum for policy A3. Using the higher value of the odds ratio for risk of GP consultation due to GI (which is associated with breastfeeding being less effective in reducing GI case) reduces potential cost savings in primary care by 58%. In this case the potential cost savings for policy A1 fall from £140,000 to £60,000 per year and in the most optimistic scenario (policy A3) potential cost savings fall from £580,000 to £240,000 per year. Using the upper estimate of time for a GP visit increases potential cost savings by 47%.

Figure 13.1: Sensitivity of potential total annual costs and cost savings per year from hospital and primary care of treating GI to changes in variously defined breastfeeding rates (refers to 788,486 infants' first year of life)

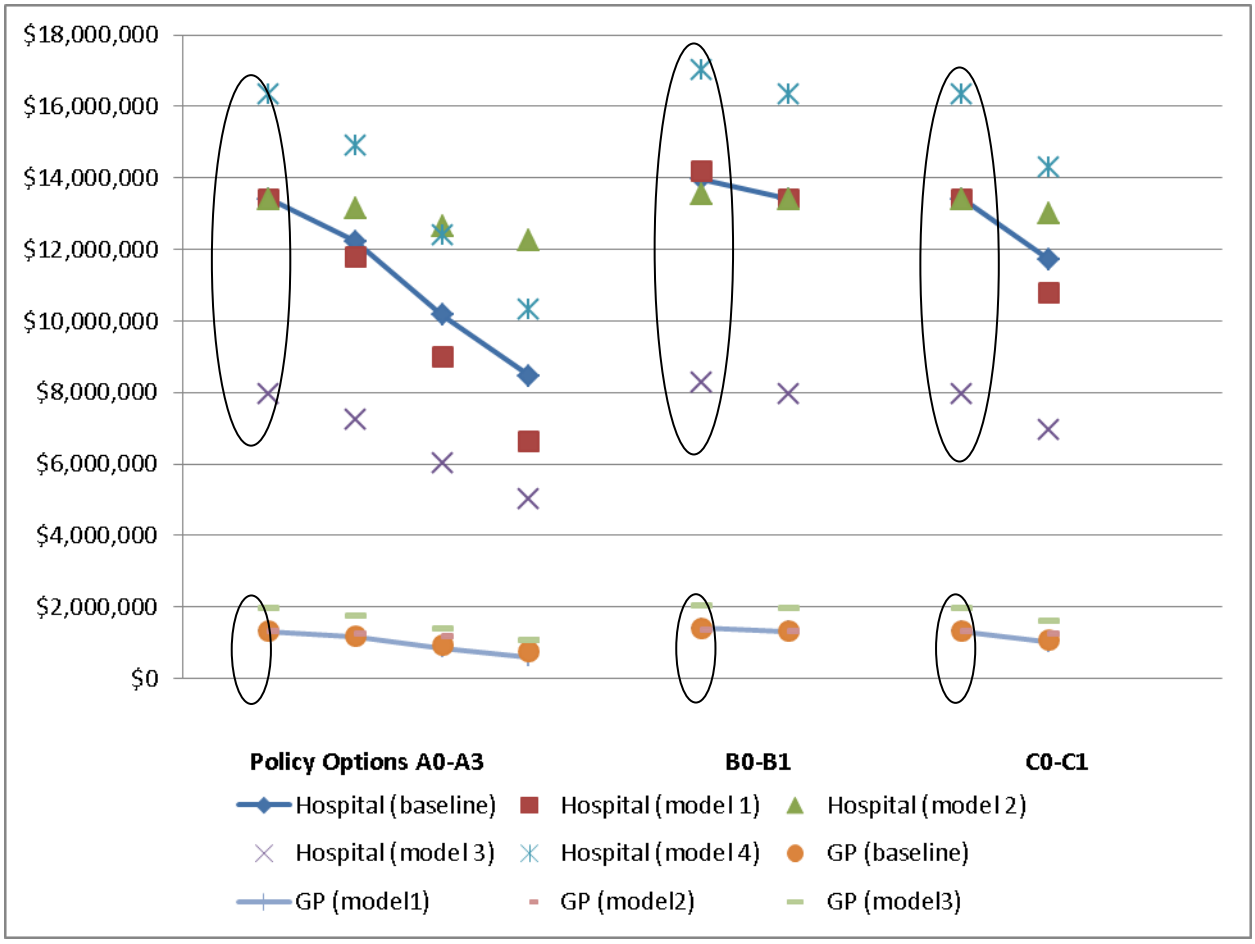


Table 13.1: Results from the sensitivity analyses (alternative values for potential hospital admission costs saved in treating gastrointestinal infections in infants less than one year old, due to increases in variously defined breastfeeding rates (refers to 788,486 infants' first year of life))

Policy options	Base case (OR=0.39 (Policy A, B); OR=0.52 (Policy C); unit cost of hospital admission=£989.44^ (Policy A,B,C)		Model 1 [Lower limit of OR=0.18 (Policy A,B); OR=0.30 (Policy C); unit cost of hospital admission=base case unit cost]			Model 2 [Upper limit of OR=0.85 (Policy A,B); OR=0.87 (Policy C); unit cost of hospital admission=base case unit cost]			Model 3 (Lower quartile of unit cost of hospital admission = £585.63^^ (Policy A,B,C); OR = base case OR			Model 4 (Upper quartile of unit cost of hospital admission = £1,206.04^^ (Policy A,B,C); OR = base case OR		
	Estimate of total hospital costs	*Estimate of total hospital costs saved**	*Estimate of total hospital costs*	*Estimate of total hospital costs saved**	*% change+*	*Estimate of total hospital costs*	*Estimate of total hospital costs saved**	*% change+*	*Estimate of total hospital costs*	*Estimate of total hospital costs saved**	*% change+*	*Estimate of total hospital costs*	*Estimate of total hospital costs saved**	*% change+*
Policy A0	£13,418,806	-	£13,418,806	-	-	£13,418,806	-	-	£7,942,333	-	-	£16,356,298	-	-
Policy A1	£12,221,725	£1,197,081	£11,784,519	£1,634,287	+36.52	£13,134,021	£284,785	-76.21	£7,233,804	£708,529	-40.81	£14,897,166	£1,459,133	+21.89
Policy A2	£10,169,585	£3,249,221	£8,982,884	£4,435,922	+36.52	£12,645,818	£772,988	-76.21	£6,019,182	£1,923,151	-40.81	£12,395,795	£3,960,503	+21.89
Policy A3	£8,459,469	£4,959,337	£6,648,188	£6,770,618	+36.52	£12,238,982	£1,179,824	-76.21	£5,006,997	£2,935,336	-40.81	£10,311,319	£6,044,979	+21.89
Policy B0	£13,974,594		£14,177,582			£13,551,028			£8,271,293			£17,033,753		
Policy B1	£13,418,806	£555,788	£13,418,806	£758,776	+36.52	£13,418,806	£132,222	-76.21	£7,942,333	£328,960	-40.81	£16,356,298	£677,455	+21.89
Policy C0	£13,418,806		£13,418,806			£13,418,806			£7,942,333			£16,356,298		
Policy C1	£11,735,356	£1,683,450	£10,800,106	£2,618,700	+55.56	£13,004,106	£414,700	-75.37	£6,945,931	£996,402	-40.81	£14,304,326	£2,051,972	+21.89

* Estimated cost-savings are relative to base case policy (Policy A0 or Policy B0 or Policy C0) for the year 2009/10

+The percentage change is the difference between base case and new estimate of cost-saving. A positive sign indicates higher cost-savings than the base case.

^ Base case unit cost estimated using Schedule 4 Combined NHS and PCT Reference Costs for non-elective activities, using the method suggested by Reference Costs Guide.

^^ Upper and Lower quartile unit cost estimated using Schedule 4 Combined NHS and PCT Reference Costs for non-elective activities, using the method suggested by Reference Costs Guide (DH 2011)

Table 13.2: Results from the sensitivity analyses (alternative values for potential GP consultation costs saved in treating gastrointestinal infections in infants less than one year old, due to increases in current breastfeeding rates (refers to 788,486 infants' first year of life))

Policy options	Base case (OR=0.28 (Policy A, B); OR=0.36 (Policy C); unit cost of GP visit=£36^ (Policy A,B,C)		Model 1 [Lower limit of OR=0.11 (Policy A,B); OR=0.18 (Policy C); unit cost of GP visit=base case unit cost]			Model 2 [Upper limit of OR=0.69 (Policy A,B); OR=0.74 (Policy C); unit cost of GP visit=base case unit cost]			Model 3 (Upper estimate of GP visit unit cost = £53^^ (Policy A,B,C); OR = base case OR		
	Estimate of total GP costs	*Estimate of total GP costs saved**	*Estimate of total GP costs*	*Estimate of total GP costs saved**	*% change+*	*Estimate of total GP costs*	*Estimate of total GP costs saved**	*% change+*	*Estimate of total GP costs*	*Estimate of total GP costs saved**	*% change+*
Policy A0	£1,329,091	-	£1,329,091	-	-	£1,329,091	-	-	£1,956,717	-	-
Policy A1	£1,188,008	£141,083	£1,152,483	£176,607	+25.18	£1,270,129	£58,962	-58.21	£1,749,011	£207,705	+47.22
Policy A2	£946,151	£382,939	£849,728	£479,363	+25.18	£1,169,051	£160,040	-58.21	£1,392,945	£563,772	+47.22
Policy A3	£744,604	£584,486	£597,432	£731,659	+25.18	£1,084,820	£244,271	-58.21	£1,096,223	£860,494	+47.22
Policy B0	£1,394,594		£1,411,087			£1,356,466			£2,053,152		
Policy B1	£1,329,091	£65,503	£1,329,091	£81,996	+25.18	£1,329,091	£27,375	-58.21	£1,956,717	£96,435	+47.22
Policy C0	£1,329,091		£1,329,091			£1,329,091			£1,956,717		
Policy C1	£1,096,183	£232,907	£1,013,787	£315,304	+35.38	£1,244,086	£85,005	-63.50	£1,613,826	£342,891	+47.22

* Estimated cost-savings are relative to base case policy for the year 2009/10.

+The percentage change is the difference between base case and new estimate of cost-saving. A positive sign indicates higher cost-savings than the base case.

^ Base case unit cost is £36 in 2009/10 & refers to per surgery consultation lasting 11.7 minutes. The figure is with qualification costs and also includes direct care staff costs.

^^ The upper estimate of unit cost is £53 in 2009/10 and refers to per clinic consultation lasting 17.2 minutes. The figure is with qualification costs and includes direct care staff costs.

Lower respiratory tract infection (LRTI) – sensitivity analyses

Deterministic sensitivity analyses assessed the impact on the estimated cost-savings of two key input parameters: the odds ratio for risk of hospitalisation for lower respiratory tract infections (LRTI) and unit costs of treating LRTI. These parameters were selected to capture the changes both in outcome (expected number of LRTI cases) and in costs to treat those cases. The base case estimate was altered, one at a time, in the following order:

- Change mean value of the odds ratio for risk of hospitalisation for LRTI to its lowest 95% confidence interval value
- Change mean value of the odds ratio for risk of hospitalisation for LRTI to its highest 95% confidence interval value
- Change national average unit cost of hospital admission for LRTI to lower quartile
- Change national average unit cost of hospital admission for LRTI to upper quartile
- Change unit cost of GP visit (based on 11.7 minutes) to unit cost of GP visit (based on 17.2 minutes)
- Equalised value of odds ratio for risk of hospitalisation for 'exclusive breastfeeding' and 'any breast feeding' (i.e. a decrease in OR for 'exclusive breastfeeding' from 0.70 to 0.67 and vice versa) as effectiveness data did not indicate significant difference.
- Equalised value of odds ratio for risk of GP consultation for 'exclusive breastfeeding' and 'any breast feeding' (i.e. a decrease in OR for 'exclusive breastfeeding' from 0.69 to 0.65 and vice versa) as effectiveness data did not indicate significant difference

Table 13.3 (parts 1 and 2), Table 13.4 (parts 1 and 2) and Figure 13.2 show the impact of the new estimates run in the sensitivity analyses relative to base case cost-savings. A positive % change (in Tables 13.3 and 13.4) indicates higher cost-savings for a new estimate. In the sensitivity analysis of the ORs for risk of hospitalisation for different rates and definitions of breastfeeding, the same rates across the same type of policies (i.e. A1-A3) would be expected but different rates would be expected between scenarios (i.e. A vs. B or C). This is because the number of cases prevented by different policies will not be proportionate. However the % change figures for the sensitivity analysis of unit cost do not change because change in total cost is the same as the proportional change in unit cost.

The results of the sensitivity analysis on saved costs from hospitalisation (Table 13.3) show that using the lower value of the odds ratio for risk of hospitalisation due to LRTI (which is associated with breastfeeding being more effective in reducing the number of LRTI cases) increases potential cost savings by 73%. Thus potential cost savings increase: from £2 million to £4million per annum for policy A1; from £5.8 million to £10 million per annum for policy A2; and from £9 million to £15 million per annum for policy A3. Using the higher value of the odds ratio for risk of hospitalisation due to LRTI (which is associated with breastfeeding being less effective in reducing LRTI cases) reduces potential cost savings by 93%. In this case the potential cost savings for policy A1 fall from £2 million to £141,000 per year and in the most optimistic scenario (policy A3) potential cost savings fall from £9 million to £0.5 million per year. Using the lower quartile of hospital costs reduces all potential hospital cost savings by 31% and using the higher quartile increases all potential hospital cost savings by 20%.

Using the lower value of the odds ratio for risk of GP consultation due to LRTI (which is associated with breastfeeding being more effective in reducing LRTI case) increases potential

cost savings by 74% (Table 13.4). Thus potential cost savings in primary care increase: from £300,000 to £500,000 per annum for policy A1; from £800,000 to £1.4 million per annum for policy A2; and from £1.2 million to £2 million per annum for policy A3. Using the higher value of the odds ratio for risk of GP consultation due to LRTI (which is associated breastfeeding being less effective in reducing LRTI case) indicates that there would be no cost savings in primary care, as the OR=1. Using the upper estimate of time for a GP visit increases potential cost savings by 47%. Increasing the cost of GP consultations by assuming longer average consultation times increases potential saved costs for primary care by 47%.

Figure 13.2: Sensitivity of potential total annual costs and cost savings per year from hospital and primary care of treating LRTI changes in variously defined breastfeeding rates (refers to 788,486 infants' first year of life)

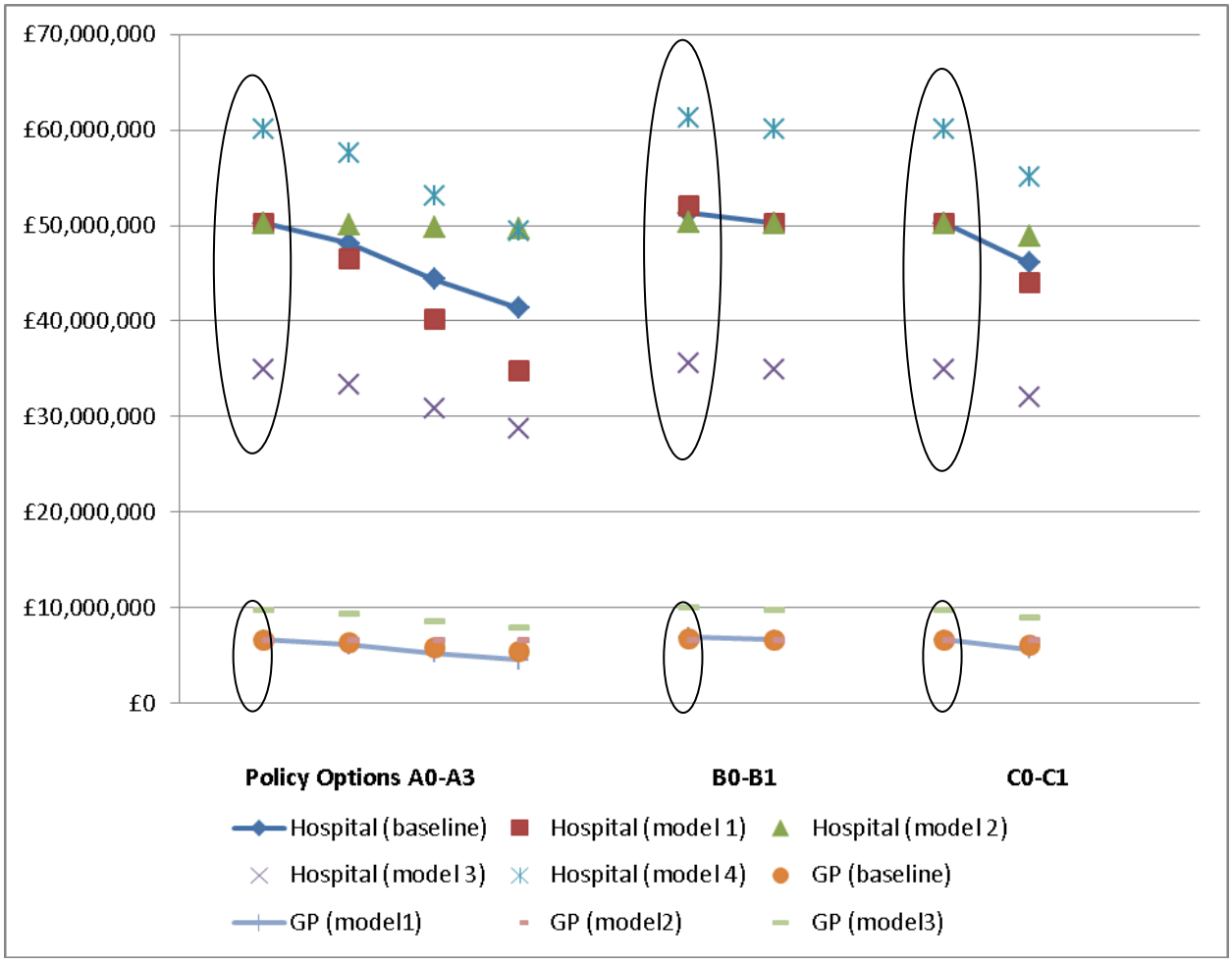


Table 13.3 (part 2) summarises the findings of the equalised odds ratios for hospitalisations for the policy options affected. It shows that the potential cost-savings from hospitalisations under policy C0-C1 decreased by 9.8% from £4.2 million to £3.7 million per year when the odds ratios were equalised at 0.70 (the value of the OR for 'exclusive breastfeeding'). The potential cost-savings from hospitalisations under policy A0-A3 and B0-B1 increased by 10.2% when the odds ratios were equalised at 0.67 (the OR for 'any breastfeeding'). The impact of equalising the

odds ratios for GP consultations (from 0.69 to 0.65 [15]and vice versa[16]) for exclusive and any breastfeeding was a respective decrease by 12% (see column 6) and increase of 13% (see column 9) on potential costs saved (Table 13.4 part 2).

[15] Baseline to model 4
[16] Baseline to model 5

Table 13.3 Part 1 (models 1-4): Results from the sensitivity analysis (alternative values for potential hospital admission costs saved in treating lower respiratory tract infections in infants less than one year old, due to increase in variously defined breastfeeding rates (refers to 788,486 infants' first year of life))

Policy options	Baseline (OR=0.70 (Policy A, B); OR=0.67 (Policy C); unit cost of hospital admission=£1078.42^ (Policy A,B,C)		Model 1 [Lower limit of OR=0.49 (Policy A,B); OR=0.52 (Policy C); unit cost of hospital admission=baseline unit cost]			Model 2 [Upper limit of OR=0.98 (Policy A,B); OR=0.88 (Policy C); unit cost of hospital admission=baseline unit cost]			Model 3 (Lower quartile of unit cost of hospital admission = £749.14^^ (Policy A,B,C); OR = baseline OR			Model 4 (Upper quartile of unit cost of hospital admission = £1,289.80^^ (Policy A,B,C); OR = baseline OR		
	Estimate of total hospital costs	*Estimate of total hospital costs saved**	*Estimate of total hospital costs*	*Estimate of total hospital costs saved**	*Estimate of total hospital costs*	*Estimate of total hospital costs*	*Estimate of total hospital costs saved**	*% change+*	*Estimate of total hospital costs*	*Estimate of total hospital costs saved**	*% change+*	*Estimate of total hospital costs*	*Estimate of total hospital costs saved**	*% change+*
Policy A0	£50,253,643	-	£50,253,643	-	-	£50,253,643	-	-	£34,909,476	-	-	£60,103,988	-	-
Policy A1	£48,097,715	£2,155,927	£46,532,695	£3,720,948	72.59	£50,112,735	£140,907	-93.46	£33,411,827	£1,497,649	-30.53	£57,525,472	£2,578,516	19.60
Policy A2	£44,401,839	£5,851,803	£40,153,927	£10,099,716	72.59	£49,871,179	£382,463	-93.46	£30,844,430	£4,065,046	-30.53	£53,105,158	£6,998,830	19.60
Policy A3	£41,321,943	£8,931,700	£34,838,287	£15,415,356	72.59	£49,669,883	£583,760	-93.46	£28,704,932	£6,204,544	-30.53	£49,421,563	£10,682,425	19.60
Policy B0	£51,254,609		£51,981,226			£50,319,064			£35,604,813			£61,301,156		
Policy B1	£50,253,643	£1,000,966	£50,253,643	£1,727,583	72.59	£50,253,643	£65,421	-93.46	£34,909,476	£695,337	-30.53	£60,103,988	£1,197,168	19.60
Policy C0	£50,253,643		£50,253,643			£50,253,643			£34,909,476			£60,103,988		
Policy C1	£46,096,420	£4,157,222	£43,949,095	£6,304,548	51.65	£48,823,745	£1,429,897	-65.60	£32,021,596	£2,887,879	-30.53	£55,131,898	£4,972,090	19.60

* Estimated cost-savings are relative to base case policy (Policy A0 or Policy B0 or Policy C0) for the year 2009/10

+The percentage change is the difference between base case and new estimate of cost-saving. A positive sign indicates higher cost-savings than the base case.

^ Base case unit cost estimated using Schedule 4 Combined NHS and PCT Reference Costs for non-elective activities, using the method suggested by Reference Costs Guide.

^^ Upper and Lower quartile unit cost estimated using Schedule 4 Combined NHS and PCT Reference Costs for non-elective activities, using the method suggested by Reference Costs Guide (DH 2011)

Table 13.3 Part 2 (models 5 and 6): Results from the sensitivity analyses (alternative values for potential hospital admission costs saved in treating LRTI in infants less than one year old, due to increase in variously defined breastfeeding rates (refers to 788,486 infants' first year of life)

Policy options	Baseline (OR=0.70 (Policy A, B); OR=0.67 (Policy C); unit cost of hospital admission=£1078.42^ (Policy A,B,C)		Model 5 [OR for risk hospitalisation for LRTI for 'EBF' and 'any BF' equalised at 0.70; unit cost of hospital admission=baseline unit cost]~			Model 6 [OR for risk hospitalisation for LRTI for 'EBF' and 'any BF' equalised at 0.67; unit cost of hospital admission=baseline unit cost]~		
	Estimate of total hospital costs	*Estimate of total hospital costs saved**	*Estimate of total hospital costs*	*Estimate of total hospital costs saved**	*% change+*	*Estimate of total hospital costs*	*Estimate of total hospital costs saved**	*% change+*
Policy A0	£50,253,643	-			-	£50,253,643	-	-
Policy A1	£48,097,715	£2,155,927				£47,877,024	£2,376,618	10.24
Policy A2	£44,401,839	£5,851,803				£43,802,822	£6,450,821	10.24
Policy A3	£41,321,943	£8,931,700				£40,407,653	£9,845,990	10.24
Policy B0	£51,254,609					£51,357,072		
Policy B1	£50,253,643	£1,000,966				£50,253,643	£1,103,430	10.24
Policy C0	£50,253,643		£50,253,643					
Policy C1	£46,096,420	£4,157,222	£46,504,993	£3,748,650	-9.83			

~The blank cells in the table mean that the predicted estimates are the same as those at baseline. This is because the OR used to obtain these predictions is exactly the same as the OR used in the baseline.

* Estimated cost-savings are relative to base case policy (Policy A0 or Policy B0 or Policy C0) for the year 2009/10

+The percentage change is the difference between base case and new estimate of cost-saving. A positive sign indicates higher cost-savings than the base case.

^ Base case unit cost estimated using Schedule 4 Combined NHS and PCT Reference Costs for non-elective activities, using the method suggested by Reference Costs Guide.

^^ Upper and Lower quartile unit cost estimated using Schedule 4 Combined NHS and PCT Reference Costs for non-elective activities, using the method suggested by Reference Costs Guide (DH 2011)

Table 13.4 Part 1 (models 1 to 3): Results from the sensitivity analysis (alternative values for potential GP consultation costs saved in treating lower respiratory tract infections in infants less than one year old, due to increase in variously defined breastfeeding rates (refers to 788,486 infants' first year of life)

Policy options	Baseline (OR=0.69 (Policy A, B); OR=0.65 (Policy C); unit cost of GP visit=£36^ (Policy A,B,C)		Model 1 [Lower limit of OR=0.47 (Policy A,B); OR=0.43 (Policy C); unit cost of GP visit=baseline unit cost]			Model 2 [Upper limit of OR=1.0 (Policy A,B); OR=0.96 (Policy C); unit cost of GP visit=baseline unit cost]			Model 3 (Upper estimate of GP visit unit cost = £53^^ (Policy A,B,C); OR = baseline OR		
	Estimate of total GP costs	*Estimate of total GP costs saved**	*Estimate of total GP costs*	*Estimate of total GP costs saved**	*% change+*	*Estimate of total GP costs*	*Estimate of total GP costs saved**	*% change+*	*Estimate of total GP costs*	*Estimate of total GP costs saved**	*% change +*
Policy A0	£6,651,445	-	£6,651,445	-	-	£6,651,445	-	-	£9,792,406	-	-
Policy A1	£6,356,369	£295,076	£6,138,892	£512,553	73.70	£6,651,445	£0	-100.00	£9,357,988	£434,417	47.22
Policy A2	£5,850,525	£800,920	£5,260,230	£1,391,215	73.70	£6,651,445	£0	-100.00	£8,613,273	£1,179,133	47.22
Policy A3	£5,428,988	£1,222,457	£4,528,012	£2,123,434	73.70	£6,651,445	£0	-100.00	£7,992,677	£1,799,729	47.22
Policy B0	£6,788,445		£6,889,416			£6,651,445			£9,994,099		
Policy B1	£6,651,445	£137,000	£6,651,445	£237,971	73.70	£6,651,445	£0	-100.00	£9,792,406	£201,694	47.22
Policy C0	£6,651,445		£6,651,445			£6,651,445			£9,792,406		
Policy C1	£6,064,660	£586,785	£5,634,531	£1,016,915	73.30	£6,589,634	£61,811	-89.47	£8,928,528	£863,878	47.22

* Estimated cost-savings are relative to base case policy for the year 2009/10.

+The percentage change is the difference between base case and new estimate of cost-saving. A positive sign indicates higher cost-savings than the base case.

^ Base case unit cost is £36 in 2009/10 & refers to per surgery consultation lasting 11.7 minutes. The figure is with qualification costs and also includes direct care staff costs.

^^ The upper estimate of unit cost is £53 in 2009/10 and refers to per clinic consultation lasting 17.2 minutes. The figure is with qualification costs and includes direct care staff costs.

Table 13.4 Part 2 (models 4 and 5): Results from the sensitivity analysis (alternative values for potential GP consultation costs saved in treating LRTI in infants less than one year old, due to increase in variously defined breastfeeding rates (refers to 788,486 infants' first year of life))

Policy options	Baseline (OR=0.69 (Policy A, B); OR=0.65 (Policy C); unit cost of GP visit=£36^ (Policy A,B,C)		Model 4 [OR for risk GP consultation for LRTI for 'EBF' and 'any BF' equalised at 0.69; unit cost of GP consultation=baseline unit cost]~			Model 5 [OR for risk GP consultation for LRTI for 'EBF' and 'any BF' equalised at 0.65; unit cost of GP consultation=baseline unit cost]~		
	Estimate of total GP costs	*Estimate of total GP costs saved**	*Estimate of total GP costs*	*Estimate of total GP costs saved**	*% change+*	*Estimate of total GP costs*	*Estimate of total GP costs saved**	*% change+*
Policy A0	£6,651,445	-				£6,651,445	-	-
Policy A1	£6,356,369	£295,076				£6,317,339	£334,106	13.23
Policy A2	£5,850,525	£800,920				£5,744,585	£906,860	13.23
Policy A3	£5,428,988	£1,222,457				£5,267,290	£1,384,155	13.23
Policy B0	£6,788,445					£6,806,566		
Policy B1	£6,651,445	£137,000				£6,651,445	£155,121	13.23
Policy C0	£6,651,445		£6,651,445					
Policy C1	£6,064,660	£586,785	£6,137,355	£514,090	-12.39			

~The blank cells in the table mean that the predicted estimates are the same as those at baseline. This is because the OR used to obtain these predictions is exactly the same as the OR used in the baseline.

* Estimated cost-savings are relative to base case policy (Policy A0 or Policy B0 or Policy C0) for the year 2009/10

+The percentage change is the difference between base case and new estimate of cost-saving. A positive sign indicates higher cost-savings than the base case.

^ Base case unit cost estimated using Schedule 4 Combined NHS and PCT Reference Costs for non-elective activities, using the method suggested by Reference Costs Guide.

^^ Upper and Lower quartile unit cost estimated using Schedule 4 Combined NHS and PCT Reference Costs for non-elective activities, using the method suggested by Reference Costs Guide (DH 2011)

Acute otitis media – sensitivity analysis

Deterministic sensitivity analyses assessed the impact on the estimated cost-savings of two key input parameters: the odds ratio for risk of GP consultations for acute otitis media (AOM) and unit costs of treating AOM. These parameters were selected to capture the changes in both outcomes (expected number of AOM cases) and costs to treat those cases. The base case estimate was altered, one at a time, in the following order:

- Change mean value of the odds ratio for risk of GP consultations for AOM to its lowest 95% confidence interval value
- Change mean value of the odds ratio for risk of GP consultations for AOM to its highest 95% confidence interval value
- Change unit cost of GP visit (based on 11.7 minutes) to unit cost of GP visit (based on 17.2 minutes)
- Equalised value of odds ratio for risk of GP visit for 'exclusive breastfeeding' and 'any breast feeding' (i.e. a decrease in OR for 'exclusive breastfeeding' from 0.5 to 0.4 and vice versa) as effectiveness data did not indicate a statistically significant difference.

Table 13.5 and Figure 13.3 show the impact of the new estimates run in the sensitivity analyses relative to base case cost-savings. A positive % change (in Table 6) indicates higher cost-savings for a new estimate. In the sensitivity analysis of the ORs for risk of GP consultation for different rates and definitions of breastfeeding, the same rates across the same type of policies (i.e. A1-A3) would be expected but different rates would be expected between scenarios (i.e. A vs. B or C). This is because the number of cases saved by different policies will not be proportionate. However the % change figures for the sensitivity analysis of unit cost do not change because change in total cost change is the same as the proportional change in unit cost.

The results of the sensitivity analysis on saved costs from GP consultations (Table 13.5) show that using the lower value of the odds ratio for risk of GP consultations due to AOM (associated with breastfeeding being more effective in reducing AOM cases) increases potential cost savings by 27%. Thus potential cost savings increase: from £0.28 million to £0.35 million per annum for policy A1; from £0.76 million to £0.96 million per annum for policy A2; and from £1.2 million to £1.5 million per annum for policy A3. Using the higher value of the odds ratio for risk of GP consultations due to AOM (associated with breastfeeding being less effective in reducing AOM cases) reduces potential cost savings by 41%. In this case the potential cost savings for policy A1 fall from £0.28 million to £0.17 million per year and in the most optimistic scenario (policy A3) potential cost savings fall from £1.2 million to £0.7 million per year. Using the upper estimate of time for a GP visit increases potential cost savings by 47%.

Table 13.5 also summarises the findings of the equalised odds ratios for GP consultations for the policy options affected. It shows that the potential cost-savings from GP consultations under policy C0-C1 decreased by 19% from £0.62 million to £0.51 million per year when OR were equalised at 0.5 (the value of OR for 'exclusive breastfeeding'). The potential cost-savings from GP consultations under policy A0-A3 and B0-B1 increased by 21% when the odds ratios were equalised at 0.4 (the OR for 'any breastfeeding').

Figure 13.3: Sensitivity of total annual costs and potential cost savings per year in primary care from treating AOM to changes in variously defined breastfeeding rates (refers to 788,486 infants' first year of life)

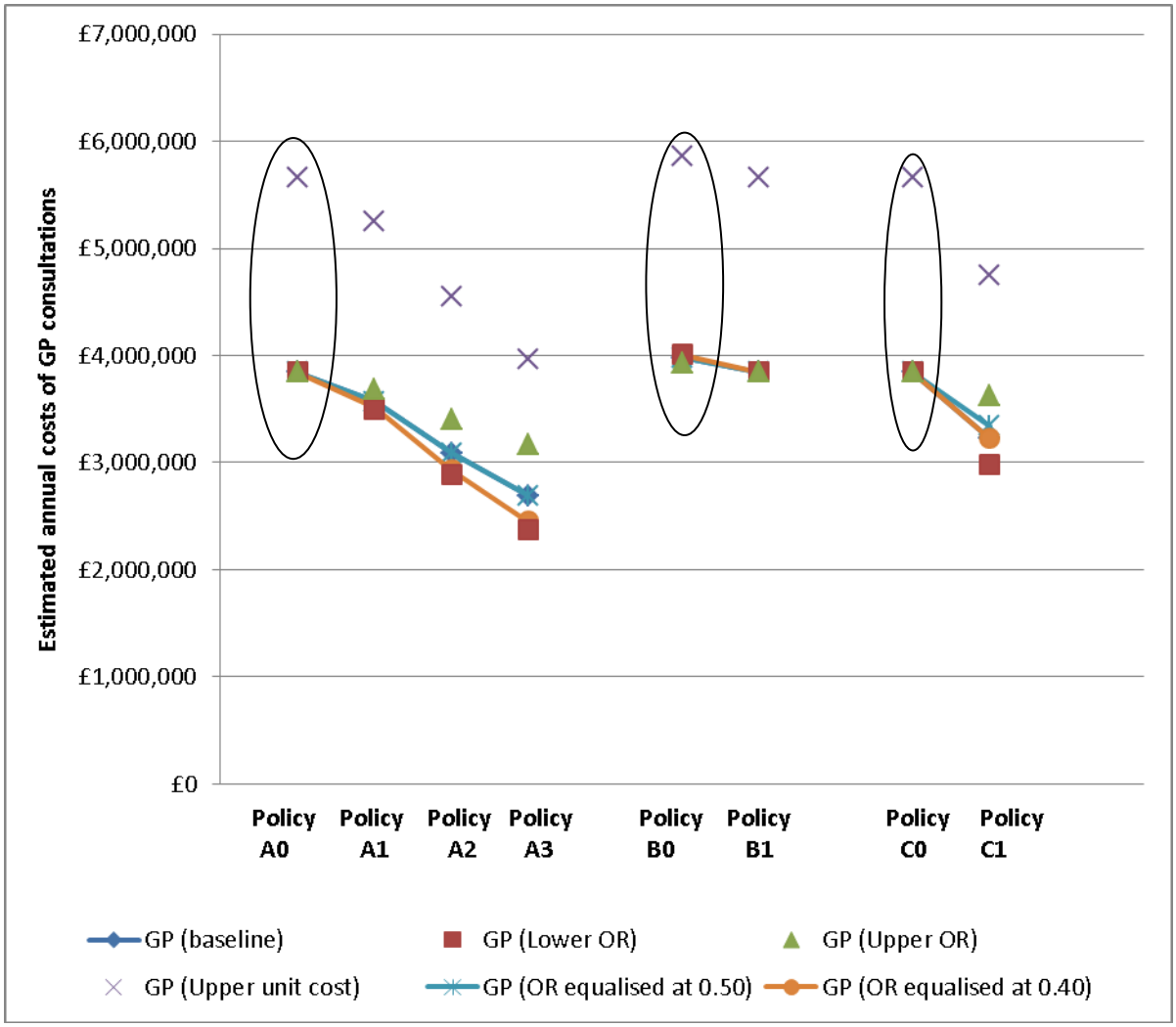


Table 13.5: Results from the sensitivity analysis (alternative values for potential GP consultation costs saved in treating otitis media in infants less than one year old, due to increase in current breastfeeding rates (refers to 788,486 infants' first year of life)

Policy options	Baseline (OR=0.50 (Policy A, B); OR=0.40 (Policy C); unit cost of GP visit=£36^ (Policy A,B,C)		Model 1 [Lower limit of OR=0.37 (Policy A,B); OR=0.21 (Policy C); unit cost of GP visit=baseline unit cost]			Model 2 [Upper limit of OR=0.70 (Policy A,B); OR=0.76 (Policy C); unit cost of GP visit=baseline unit cost]			Model 3 (Upper estimate of GP visit unit cost = £53^^ (Policy A,B,C); OR = baseline OR			Model 4 [OR equalised at 0.50; unit cost of GP consultation=baseline unit cost]			Model 5 [OR equalised at 0.40; unit cost of GP consultation=baseline unit cost]		
	Estimate of total GP costs	*Estimate of total GP costs saved**	*Estimate of total GP costs*	*Estimate of total GP costs saved**	*% change +*	*Estimate of total GP costs*	*Estimate of total GP costs saved**	*% change +*	*Estimate of total GP costs*	*Estimate of total GP costs saved**	*% change +*	*Estimate of total GP costs*	*Estimate of total GP costs saved**	*% change +*	*Estimate of total GP costs*	*Estimate of total GP costs saved**	*% change +*
A0	£3,847,960	-	£3,847,960	-	-	£3,847,960	-	-	£5,665,052	-	-				£3,847,960	-	-
A1	£3,568,833	£279,127	£3,492,912	£355,048	27.20	£3,682,879	£165,081	-40.86	£5,254,116	£410,936	47.22				£3,510,561	£337,399	20.88
A2	£3,090,331	£757,629	£2,884,259	£963,701	27.20	£3,399,883	£448,077	-40.86	£4,549,653	£1,115,399	47.22				£2,932,162	£915,798	20.88
A3	£2,691,578	£1,156,382	£2,377,048	£1,470,912	27.20	£3,164,053	£683,907	-40.86	£3,962,601	£1,702,451	47.22				£2,450,162	£1,397,798	20.88
B0	£3,977,555		£4,012,804			£3,924,605			£5,855,844						£4,004,610		
B1	£3,847,960	£129,595	£3,847,960	£164,844	27.20	£3,847,960	£76,645	-40.86	£5,665,052	£190,792	47.22				£3,847,960	£156,650	20.88
C0	£3,847,960		£3,847,960			£3,847,960			£5,665,052			£3,847,960					
C1	£3,223,232	£624,728	£2,976,715	£871,245	39.46	£3,621,995	£225,965	-63.83	£4,745,314	£919,738	47.22	£3,342,228	£505,732	-19.05			

~The blank cells in the table mean that the predicted estimates are the same as those at baseline. This is because the OR used to obtain these predictions is exactly the same as the OR used in the baseline.

* Estimated cost-savings are relative to base case policy for the year 2009/10.

+The percentage change is the difference between base case and new estimate of cost-saving. A positive sign indicates higher cost-savings than the base case.

^ Base case unit cost is £36 in 2009/10 & refers to per surgery consultation lasting 11.7 minutes. The figure is with qualification costs and also includes direct care staff costs.

^^ The upper estimate of unit cost is £53 in 2009/10 and refers to per clinic consultation lasting 17.2 minutes. The figure is with qualification costs and includes direct care staff costs.

Necrotising enterocolitis (NEC) in babies in neonatal units: sensitivity analyses

Deterministic sensitivity analyses assessed the impact on the estimated cost-savings of two key input parameters: the odds ratio for risk of NEC and unit costs of treating NEC. These parameters were selected to capture the changes in both outcomes (expected number of NEC cases) and costs to treat those cases. The base case estimate was altered, one at a time, in the following order:

- Change mean value of the odds ratio for risk of NEC to its lowest 95% confidence interval value
- Change mean value of the odds ratio for risk of NEC to its highest 95% confidence interval value
- Change national average unit cost of a bed day in neonatal units to lower quartile
- Change national average unit cost of a bed day in neonatal units to upper quartile
- Change national average unit cost of a NEC surgery to lower quartile
- Change national average unit cost of a NEC surgery to upper quartile

Table 13.6 and Figure 13.4 show the impact of the new estimates from the sensitivity analyses relative to base case cost-savings. A positive % change (in Table 3) indicates higher cost-savings for a new estimate. In the sensitivity analysis of the ORs for risk of NEC for different rates of any breastmilk feeding in neonatal units, the same rates across the policies (i.e. D1-D3) would be expected. This is because the number of cases prevented saved by different policies will be proportionate.

Also, the % change figures for the sensitivity analysis of unit cost do not change because change in total cost is the same as the proportional change in unit cost.

The results of the sensitivity analysis on saved costs from hospitalisation (Table 7) show that using the lower value of the odds ratio for risk of NEC (which is associated with breastmilk feeding being more effective in reducing the number of cases of NEC) increases potential cost savings by 24%. Thus potential cost savings increase: from £3 million to £3.7 million per annum for policy D1; from £6.6 million to £8.2 million per annum for policy D2; and from £10.2 million to £12.6 million per annum for policy D3. Using the higher value of the odds ratio for risk of NEC (which is associated with breastmilk feeding being less effective in reducing the number of cases of NEC) reduces potential cost savings by 72%. In this case the potential cost savings for policy D1 fall from £3 million to £0.83 million per year and in the most optimistic scenario (policy D3) potential cost savings fall from £10 million to £2.8 million per year. Using the lower quartile of bed-day costs reduces all potential hospital cost savings by 17% and using the higher quartile of bed-day costs increases all potential hospital cost savings by 15%. Using the lower quartile of surgery costs reduces all potential hospital cost savings by 1.4% and using the higher quartile of bed-day costs increases all potential hospital cost savings by 0.65%.

Figure 13.4 Sensitivity of potential total annual costs and cost savings per year from treating NEC to increases in the rate of any breastmilk feeding at discharge in neonatal units (refers to 79,094 neonatal admissions and 798 NEC cases in 2009/10)

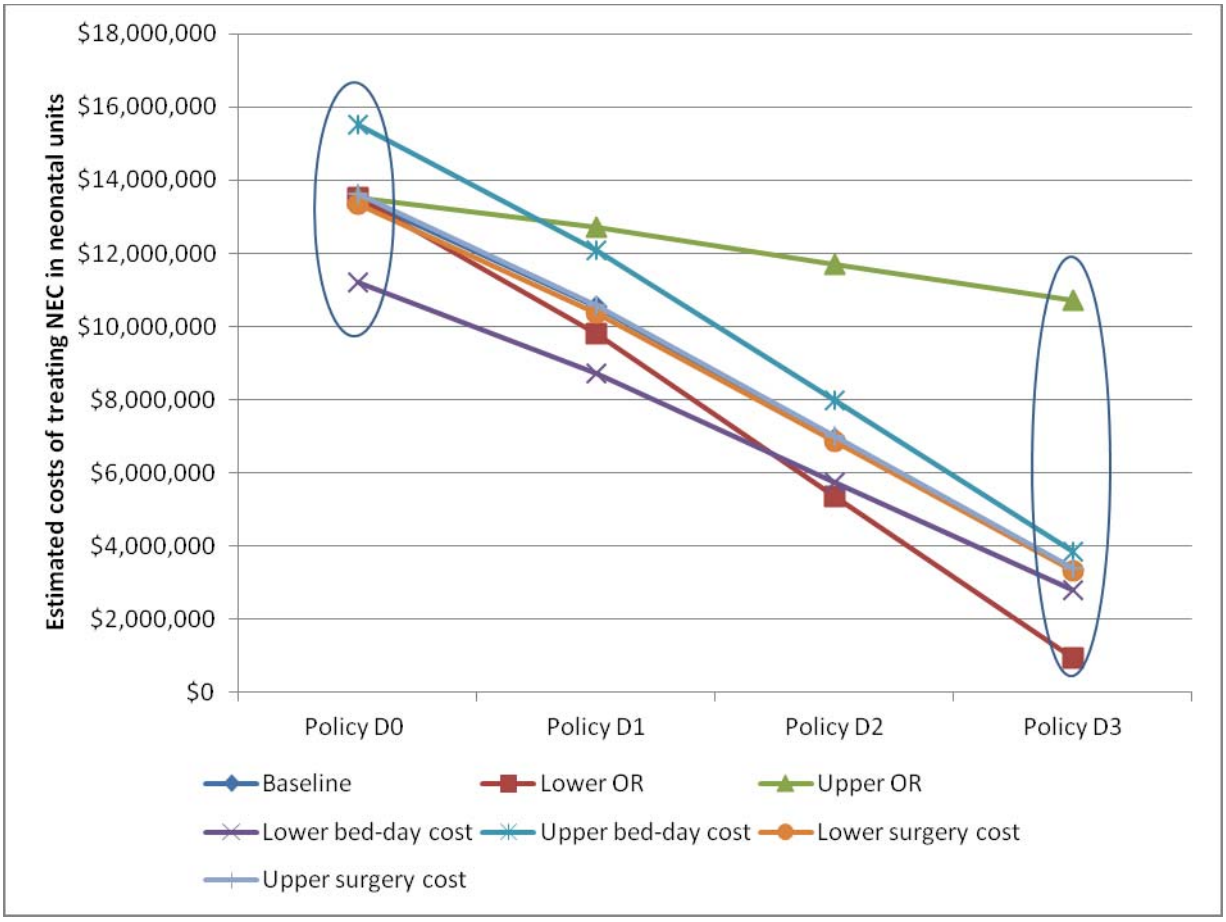


Table 13.6 Results from the sensitivity analyses (alternative values for potential costs saved in treating NEC in infants less than one year old, due to increase in rates of any breastmilk feeding (refers to 79,094 neonatal admissions and 798 NEC cases in 2009/10) (£, million 2009/10))

Policy options	Baseline (OR=0.19; unit cost of bed day=£618.34^; unit cost of NEC surgery=£1,450.07^)		Model 1 (Lower limit of OR=0.05; unit cost of bed day=baseline unit cost; unit cost of NEC surgery=baseline unit cost)			Model 2 (Upper limit of OR=0.73; unit cost of bed day=baseline unit cost; unit cost of NEC surgery=baseline unit cost)			Model 3 (OR=baseline OR; Lower quartile unit cost of bed day=£509.44^; unit cost of NEC surgery=baseline unit cost)			Model 4 (OR=baseline OR; Upper quartile unit cost of bed day=£712.17^; unit cost of NEC surgery=baseline unit cost)			Model 5 (OR=baseline OR; unit cost of bed day=baseline unit cost; Lower quartile unit of cost of NEC surgery=£689.07^)			Model 6 (OR=baseline OR; unit cost of bed day=baseline unit cost; Upper quartile unit cost of NEC surgery=£1,802.20)		
	Est. total costs	*Est. total costs saved**	*Est. total costs*	*Est. total costs saved**	*% change+*	*Est. total costs*	*Est. total costs saved**	*% change+*	*Est. total costs*	*Est. total costs saved**	*% change+*	*Est. total costs*	*Est. total costs saved**	*% change+*	*Est. total costs*	*Est. total costs saved**	*% change+*	*Est. total costs*	*Est. total costs saved**	*% change+*
Policy D0	£13.54	£0.00	£13.54	£0.00	-	£13.54	£0.00	-	£11.22	£0.00	-	£15.53	£0.00	-	£13.35	£0.00	-	£13.62	£0.00	-
Policy D1	£10.53	£3.01	£9.81	£3.73	23.9	£12.70	£0.83	-72.3	£8.72	£2.49	-17.1	£12.08	£3.45	14.8	£10.38	£2.97	-1.4	£10.59	£3.03	0.65
Policy D2	£6.94	£6.59	£5.37	£8.16	23.9	£11.71	£1.82	-72.3	£5.75	£5.46	-17.1	£7.97	£7.57	14.8	£6.85	£6.50	-1.4	£6.99	£6.63	0.65
Policy D3	£3.36	£10.17	£0.93	£12.60	23.9	£10.72	£2.82	-72.3	£2.79	£8.43	-17.1	£3.86	£11.68	14.8	£3.31	£10.03	-1.4	£3.38	£10.24	0.65

Costs figures in millions of pounds.

* Estimated cost-savings are relative to base case policy for the year 2009/10.

+The percentage change is the difference between base case and new estimate of cost-saving. A positive sign indicates higher cost-savings than the base case.

^ The figure is estimated using HRG4 Schedule 4 (NHS Trusts and PCT combined) Reference costs 2009/10.

Breast cancer in mothers – sensitivity analysis

Deterministic sensitivity analyses assessed the impact on the estimated savings of key input parameters: the odds ratio for risk of breast cancer, unit costs of treating breast cancer, utilities, discount rates, and threshold (i.e. value of a QALY). These parameters were selected to capture the changes in both outcomes (expected number of breast cancer cases) and costs to treat those cases. The base case estimate was altered, one at a time, in the following order:

- Change mean value of the odds ratio for risk of breast cancer to its lowest 95% confidence interval value
- Change mean value of the odds ratio for risk of breast cancer to its highest 95% confidence interval value
- Change average unit cost of treating breast cancer to higher end cost
- Change mean utility to lower end utility reflecting most severe breast cancer
- Change mean utility to higher end utility reflecting least severe breast cancer
- Change discount rate to 1.5%
- Change discount rate to 3.5%
- Change cost-effectiveness threshold from £20,000 to £30,000

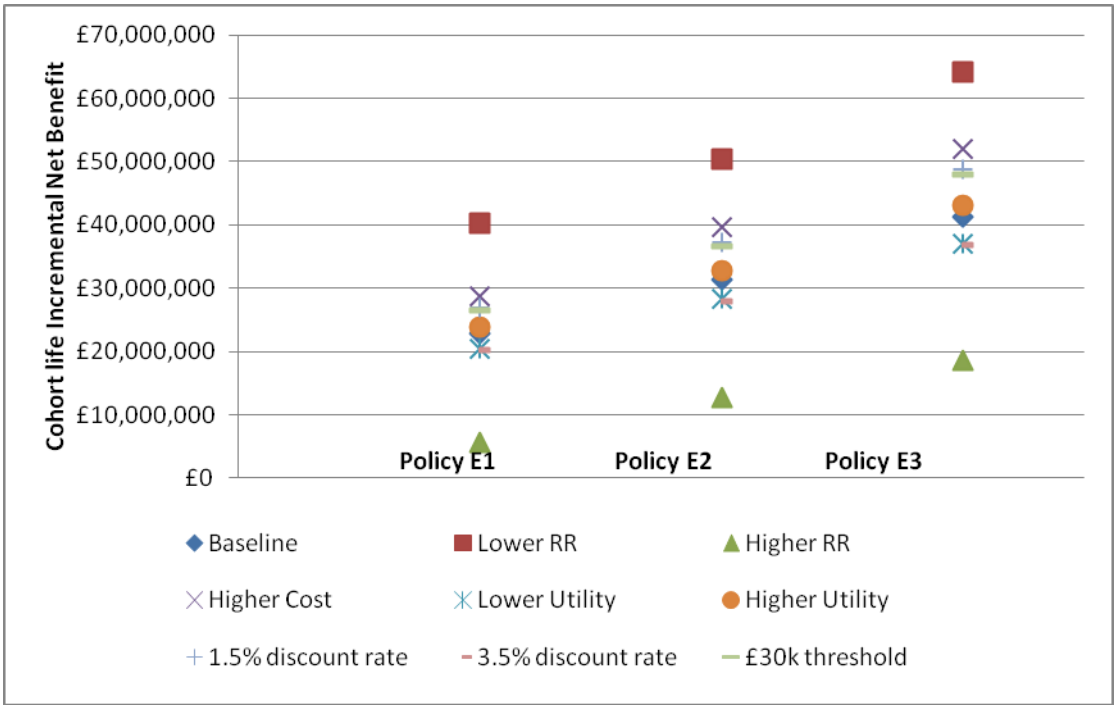
Results presented in Table 13.7 shows that potential incremental benefit changed from a baseline estimate of £23 million for Policy E1 to £40 million when effect size of breastfeeding on breast cancer was assumed to be higher and to £6 million when it was assumed to be lower. Likewise, incremental benefit went up from £23 million to £29 million when average cost of treating a breast cancer was assumed to be higher and to just above £26 million when the threshold was assumed to be £30,000.

This pattern remained for other policy scenarios as well (Table 13.7 and Figure 13.5)

Table 13.7: Alternative values for potential incremental benefit in treating breast cancer relative to Policy E0: results from sensitivity analysis (2009/10 prices)

	Policy E1	Policy E2	Policy E3
Baseline	£22,761,127	£31,420,702	£41,258,830
Lower RR	£40,240,637	£50,295,539	£64,249,628
Higher RR	£5,596,045	£12,820,449	£18,647,404
Higher Cost	£28,690,942	£39,606,543	£52,007,736
Lower Utility	£20,450,095	£28,230,428	£37,069,650
Higher Utility	£23,787,816	£32,838,000	£43,119,897
1.5% discount rate	£26,956,499	£37,212,223	£48,863,732
3.5% discount rate	£20,265,127	£27,975,087	£36,734,359
£30k threshold	£26,473,453	£36,545,400	£47,988,121

Figure 13.5: Sensitivity of potential incremental benefit to increase in the rate of breastfeeding (refers to 313,817 primiparous women in 2009/10)



Appendix 14

Lancashire Children's Trust
Statement of Strategic Intent for Infant Feeding in Lancashire (TEXT ONLY)

This document was produced for the Lancashire Infant Mortality Leads Meeting (subgroup of the Lancashire Children's Trust reporting via the Be Healthy Themed Group) by a Task and Finish group comprising Infant Feeding specialists in Lancashire. With thanks to Francesca Entwistle (Principal Lecturer, Professional Lead Midwifery, Link Lecturer East & North Herts NHS Trust) and Professor Mary J. Renfrew (Director, Mother and Infant Research Unit, University of York).

1. Maternity services in both the hospital and community setting to gain the World Health Organisation / UNICEF Baby Friendly Initiative accreditation 'Ten steps to successful breastfeeding' and the 'Seven Point Plan for sustaining breastfeeding in the community'
2. Peer, 'mother to mother' support programmes to be implemented alongside health professional care
3. Universities to gain UNICEF UK Baby Friendly Initiative accreditation in pre-registration midwifery and post-registration health visiting programmes
4. Neonatal networks trained to implement effective breastfeeding support for sick and premature babies
5. Provision of 'donor' breast milk where a mother is unable to breastfeed her baby and including the most vulnerable such as premature babies, those in neonatal units and babies aged less than 6 months who are to be adopted
6. A robust and critical support service to filter harmful advertising and marketing of formula milks
7. Strategic leadership, local and regional, to implement evidence-based policy and practice, including those areas that impact on infant feeding practice such as where babies sleep
8. 'Breastfeeding welcome' employer, community and public spaces
9. Schools programmes that promote breastfeeding
10. Services that support women who are artificially feeding their babies to minimise the risks

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Appendix 15

Describing and costing the Lancashire programme

Description of components of the Lancashire programme

1. Maternity services in both the hospital and community setting to gain the World Health Organisation/UNICEF Baby Friendly Initiative accreditation 'Ten steps to successful breastfeeding' and the 'Seven Point Plan for sustaining breastfeeding in the community'

The WHO/UNICEF Baby Friendly Initiative (BFI) is a structured quality improvement programme for hospitals and primary care trusts that addresses staff training, support for women, and removal of practices that are harmful to the establishment and maintenance of breastfeeding, such as routine supplementation with breastmilk substitutes. NICE public health guidance recommends it as the minimum standard for health services. Achieving full accreditation is a staged process, starting with registering intent, progressing to a Certificate of Commitment, Stage 1 and Stage 2 assessments, until full accreditation is gained. Information about criteria and processes can be found at http://www.unicef.org.uk/BabyFriendly/About-Baby-Friendly/, as can a full listing of the status of hospitals and PCTs.

UNICEF UK BFI accreditation is becoming more common across the UK. At the end of 2008, 51 maternity units had full accreditation; in contrast, over 200 new awards were approved in 2011. By March 2012, seventy nine maternity units and PCTs had full accreditation (17%), 218 (47%) had either stage 1 or stage 2 awards, and 83 (18%) had a certificate of commitment or have registered their intent (source: UNICEF BFI).

Implementation is not consistent across the country; only 17% of maternity units and PCTs have no contact with UNICEF BFI, all in England. Table 15.1 below shows the percentage of births in UNICEF UK BFI accredited hospitals as of January 2012, showing that Scotland and Wales have a much higher percentage than England and Northern Ireland.

Table 15.1: Percentage of births in UNICEF BFI accredited hospitals in the four UK countries: from UNICEF UK BFI website, accessed 16th January 2012

Country	Percent of births in UNICEF BFI accredited hospitals
England	17%
N Ireland	61%
Scotland	71%
Wales	54%

Of the six hospitals offering maternity services in Lancashire, two already have full accreditation, one has Stage 2, and two have registered their intention to proceed. Of the five Lancashire PCTs, three have full accreditation, one is at Stage 1, and one has a Certificate of Commitment (June 2012).

Achieving BFI accreditation has not been included in our costing, as it is a priority NICE recommendation and is considered to be a fundamental part of health service provision.

2. Peer, 'mother to mother' support programmes to be implemented alongside health professional care

Good quality evidence demonstrates that peer support programmes, where women from the local community who have received basic training work together with formal health service provision, is effective in enabling women to breastfeed (Dyson et al, 2008, National Institute for Health and Clinical Excellence, 2008 updated 2011, Renfrew et al, 2012). Such schemes require adequate provision for training, support and supervision of the peer supporters. A scheme put in place in Lancashire (though now discontinued) achieved rapid improvement in breastfeeding rates (Agboado et al, 2010).

Provision of peer support has not been included in our costing, as it has been a priority NICE recommendation since 2008, and is considered to be a fundamental part of health service provision. We recognise that some localities still have not put programmes in place to offer support to all women.

3. Universities to gain UNICEF UK Baby Friendly Initiative accreditation in pre-registration midwifery and post-registration health visiting programmes

It has been recognised that the education and training of health professionals to enable women to breastfeed, including doctors, midwives and health visitors, has been inadequate for several decades, resulting in a core deficit in health professional knowledge and skills (McFadden et al, 2006). It is a requirement for midwifery education programmes to meet the infant feeding standards set by the Nursing and Midwifery Council. The UNICEF UK Baby Friendly Initiative has established an improvement programme for pre-registration education programmes for midwives and health visitors to ensure that newly qualifying staff have adequate knowledge and skills to help women to breastfeed. None of the Lancashire universities currently holds this accreditation.

As this component of the programme meets the priority NICE recommendation that health professionals should be trained in breastfeeding management, and as there are compulsory NMC infant feeding standards for midwifery programmes, this expenditure should not be seen as optional, and it has not been included in our costing.

4. Neonatal networks trained to implement effective breastfeeding support for sick and premature babies

Around 10% of babies are admitted to Special and Intensive Care settings in the UK. Families from low income backgrounds are over-represented in this group, as they are more likely to have a premature or low birth weight baby. Breastfeeding and feeding with breastmilk is especially important for these vulnerable babies, who are more likely to develop complications such as necrotising enterocolitis and sepsis, both of which have serious and sometime fatal consequences. Staff in neonatal units need additional education and training to enable them to adequately support all women to breastfeed or express breastmilk for their babies, and for women to have close and ongoing skin-to-skin kangaroo contact.

5. Provision of donor breastmilk where a mother is unable to breastfeed her baby and including the most vulnerable such as premature babies, those in neonatal units and babies aged less than six months who are to be adopted.

Women who are ill or who have particular psycho-social challenges may be unable to breastfeed or to express breastmilk for their baby; this may be a temporary problem which can be addressed with good care and support. In such circumstances, and especially for babies who are small or sick, donor breastmilk is an important substitute for mothers' own milk. It is essential that the arrangements for the procurement, storage, transport and

feeding of donor milk are of very high quality, and milk banking facilities are needed, run to the same standard as blood banks.

In 2011 Lancashire used 103 litres of donor milk, bought from three different milk banks. It is not known if the milk banks could sustain those costs if levels of demand rose, as would be likely if breastfeeding rates rose, as it is common for milk banks to rely on some degree of voluntary support.

6. A robust and critical support service to filter harmful advertising and marketing of formula milks

It is recognised that the marketing of infant formula has had a significant impact on the growth of formula use. Formula company representatives regularly visit health service premises and talk with staff about the purchase of their products. It is essential that all such discussions are based on good quality evidence rather than marketing and promotional messages. To support staff and to provide good quality information to inform the purchase and use of formula by the health services, formula companies should be required to provide standard information about their products including the evidence on which their information is based. The WHO/UNICEF BFI programme recommends that a nominated person liaise with formula representatives. A service established in Blackpool and North Lancashire has formalised this process by establishing a group to be the sole point of contact with the formula representatives, to critically examine the information that they provide, to inform the commissioning of formula products, and to disseminate evidence-based information. Known as the IFIT group (Infant Feeding Information Team), the group includes representatives from midwifery, health visiting, paediatrics, Children's Centres, and the voluntary sector. Work is ongoing to develop this service to service the whole region.

7. Strategic leadership, local and regional, to implement evidence-based policy and practice and ensure coordination of the whole programme of services.

A key component of improving services is strategic leadership. The challenge for this topic is that as a result of the lack of education and training and the socio-cultural issues described in Section 1, infant feeding is not always well understood, even by those in leadership positions. Leadership is needed both at the level of individual Trusts, and also at regional level to ensure coordination and senior support. Such leadership could then ensure the implementation of other elements of this programme. It should include an identified full time infant feeding coordinator in each Trust, and education and training for staff in key senior positions in Trusts and in regional public health roles.

A priority national recommendation is that a health professional is appointed to ensure that a consistent breastfeeding policy is implemented. This would be included in this leadership work, but it would reach more widely than that; we have therefore included 50% of the costs of this leadership.

8. 'Breastfeeding welcome' employer, community and public spaces

To address the challenges that women often encounter when breastfeeding when out of the home, work is needed to ensure public and community spaces are welcoming when they need to feed their babies. A programme to engage employers, retail outlets, transport systems etc in enabling women to breastfeed is key to this. Coordinating this work should be part of the role of the strategic leaders identified and costed in point 7. The small amount of additional costs to the business and transport sectors, for example to inform and train their staff, should be easily absorbed by them and costs are not included here.

9. Schools programmes that promote breastfeeding

It has been shown that children receive messages about infant feeding very early (Angell et al, 2011), and that children in their first years of primary school have already absorbed messages about formula and breastfeeding, including positive messages about formula and negative messages about breastfeeding. Accurate information about infant feeding is needed at different stages in the curriculum, during lessons about family, nutrition, healthy living, and childcare. This will require education and training of school teachers; these costs have not been included as they would not accrue to the health service and coordination by the strategic leaders identified in point 7.

10. Services that support women who are artificially feeding their babies to minimise the risks

The majority of babies in the UK are fed on formula, either exclusively or in part. It is important to minimise the risks of formula feeding, by encouraging good hygiene practices while storing, preparing and feeding formula. Educating and training staff to educate parents in such practices is essential, and could prevent some of the acute illness associated with not breastfeeding.

Coordination of this work would be the responsibility of the formula service costed in point 6, together with the strategic leadership costed in point 7, and some basic staff updating.

Details of costs of interventions additional to the priority activities

Training staff in neonatal units

Based on the costs of a current development programme with neonatal networks in Yorkshire and the Humber:

For one network - 1 full time NHS Band grade 7, plus costs for travel, communications etc – £5k for resources, 4 face to face study/training days for 30 staff (travel to central location, plus 4 days of time, 25 Band 7, 5 Band 8). Plus completion of three units of University of York multidisciplinary online education programme (100 staff, each £75+£100x2 = £27,500)

Total costs of training neonatal staff (one-off) = circa £117,000

Donor breast milk provision

In 2011 Lancashire used 103 litres of donor milk, bought from three different milk banks. This milk cost Lancashire £100 litre (total of £10,300), with transport costs of circa £3000. It is not known if the milk banks could sustain those costs if levels of demand rose, as would be likely if breastfeeding rates rose, as it is common for milk banks to rely on some degree of voluntary support.

Total cost of purchase and transport of donor milk per annum at current levels of use (recurring, likely to increase) = circa £13,300

As an alternative to this costing, if the demand for donor milk substantially increases, a better approach could be to establish larger-scale milk banks on a regional basis.

Costs of establishing such a service have been calculated with input from staff of the milk bank at Queen Charlotte's Hospital and are shown below.

Infant Feeding Information Team

The costs of the Blackpool and North Lancashire IFIT scheme, which provides independent information about formula to NHS Trusts, are circa £23,250 per annum.

Making this service available to the whole of Lancashire would involve some additional coordination (0.6 wte NHS Band 7) some additional travel (circa £1500), and additional administrative and information resources (circa £2000). These costs would also support the changes needed to minimise the risks of formula in point 10.

This service could be run as a centralised, national service for the NHS, in which case each region would not need to provide its own service, reducing the costs considerably at a national level.

Total costs for this service = circa £57,000 (recurring)

Strategic leadership

Costs include co-ordinators for each NHS Trust and training for senior staff.

Infant Feeding Coordinators for each Trust: 5 for hospital Trusts, 5 for community-based organisations: 10 NHS Band 7 full time posts.

Senior staff (Band 8a) across commissioning organisations (10) and senior staff in hospital Trusts (5) will need additional education and training to ensure they understand the key issues and can support and advocate for the coordination and implementation of services. Costs for completion of three units of the University of York multidisciplinary online education programme have been used as the basis of this (£75 +2x£100), to include the costs of staff time to complete these units (30 hours in total, NHS Band 8a)

Region-wide strategic leadership is also needed, as part of a broader public health leadership role: NHS Band 8c, pro-rata one sixth of their time.

Total costs for strategic leadership (recurring) = circa £518,000. We have included 50% of this in our costings, as coordination is a priority national recommendation, and many Trusts already have an Infant Feeding lead in place.

Offering women advice and information about formula feeding

Coordination of this work would be the responsibility of the formula service costed in point 6, together with the strategic leadership costed in point 7. All staff will be encouraged to complete the free RCPCH Early Years session on formula feeding. This takes about 20 minutes, and minimal commitment of time has not been costed.

No additional cost

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Set up and operational costs for a new milk bank in the UK

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January 19th 2012

As an alternative to the costing to maintain the current service as above, if the demand for donor milk substantially increases, a better approach could be to establish larger-scale milk banks on a regional basis. Costs of establishing such a service have been calculated with input from staff of the milk bank at Queen Charlotte's Hospital. The cost per litre on a recurring basis is very similar to that shown in the Lancashire costs With the additional set-up costs, this could provide a more efficient and cost-effective service, serving a larger population and with a single core staff working to agreed national standards.

There are currently 17 milk banks in the UK. These include one in Scotland and one in Northern Ireland and a newly opened (November 2011) bank in Bristol at Southmead Hospital. A small milk bank at Kingston Hospital in Surrey closed in 2011 however the hospital now obtains donor breastmilk (DBM) from another milk bank at a local tertiary hospital, situated within the same Perinatal Network.

Milk banks in the UK vary widely in terms of activity, staffing levels, funding and resources. For example in 2010 in the UK:

Number of donors recruited in 2010 (1st January – 31st December)

	< 50 donors	**51 – 100 donors**	**> 100 donors**	**Total**
No of milk banks	9	5	3	17
Range	9 – 49 donors	55 – 86 donors	120 – 184 donors	-
Total number of donors	285	369	474	1128

Volume of donor breastmilk collected in 2010

	< 100 litres	**101 – 500 litres**	**> 500 litres**	**Total**
No of milk banks	2	10	5	17
Range	26 – 33 litres	124 – 430 litres	585 – 1400 litres	-
Total volume of DBM collected	59 litres	2510 litres	4500 litres	7069 litres

The costs incurred in operating a milk bank therefore vary widely. Only two milk banks in England have a separate budget and are therefore able to account for all or most of their costs and any income.
The costs incurred when establishing a new milk bank will be dependent upon:

- Facilities available – location (work required to bring it up to the specification for a milk bank), number of storage and milk treatment rooms and office space required and new equipment to be purchased

- Expected use – access to DBM by one or more neonatal units, level of units, number of infants cared for.
- The following calculations on costs are estimates based on experience of running a milk bank:

To develop a bank that will supply 100 litres of donor milk a year to the local (funding) neonatal unit only:

- Set up costs: approximately £50,000 to include specialist equipment (see below - pasteuriser, freezers and fridges, laminar flow cabinet, milk storage and thawing boxes and containers, computerised tracking facilities, transport boxes, office equipment and furniture.) This does not include any work required to provide suitable facilities (sinks, appropriate surfaces and flooring etc) and does not include the cost of cleaners and general maintenance, power and light)
- Annual staffing and operational costs: approximately £60,000 - £75,000 a year based on two 0.5 wte band 4 / 5 pasteurising and donor recruitment staff and 0.2 wte band 7/8 manager, maintenance contracts, consumables, equipment replacement, donor screening and milk testing costs, transport costs etc.

Equipment costs (included in set up costs above)
Pasteuriser: £12,000 - £20,000 (38,000 Euros for new large scale pasteuriser from France)
Freezers: £900 - £3,500 per freezer
Fridges: £500 - £1500 per fridge
Laminar Flow cabinet: £2500
Consumables and ongoing expenses:
Tests: Blood tests per donor - approximately £100 including transport costs
Microbiology tests on milk - approximately £10 per sample including transport costs
Sterile Breastmilk Containers: 18p – 28p per container. I litre of DBM will require approximately 30 containers.

To develop a bank that operates on a larger scale recruiting at least 200 donors a year and providing 1500 litres DBM to local hospital NNU and other requesting hospital NNUs:

- Set up costs as above: approximately £150,000
- Annual staffing and operational costs: approximately £200,000 a year based on 1 wte band 8 Manager and 3 wte operational staff (bands 4/5/6), consumables, equipment replacement, donor screening and milk testing costs, transport costs etc.

Cost per litre:
£100/litre set up costs (Year 1)
£133/litre recurring costs

Appendix 16

Potential cost-savings in Lancashire

Gastroenteritis: The same economic model for gastroenteritis developed in Section 4.3 of the main report was re-run to reflect Lancashire-specific input parameters, where available (Table 16.1).

Table 16.1: Lancashire-specific input parameters used in Gastroenteritis Economic Model*

Parameter	Value	Description	Source
Reference population	13,785 infants <1 year	Lancashire live birth totals after adjusting with Lancashire neonatal-mortality rate	ONS (2010)
Breastfeeding rates	EBF at 6-week: 24% Any breastfeeding at 6 week: 33%	Average across 5 PCTs, where data was available.	ChiMat Data Atlas
Rate of gastroenteritis-related hospitalisations in <1 year	23.6 per 1000 infants <1 year	Hospitalisation rates due to gastroenteritis. Rate for the "North West" region	Infant Feeding Profile (2011)
Rate of gastroenteritis-related GP consultations in <1 year	8,215 per 100,000 infants <1 year	GP consultations rate for clinical diagnosis of intestinal infectious diseases (IID) in children <1 year. Rate for the "North" region	RCGP (2010)

*All other input parameters unchanged.

Table 16.2: Lancashire-specific policy scenarios modelled

Definition of breastfeeding and rate used in base case:	Alternative policy scenarios modelled:		
LA0: Exclusive breastfeeding (EBF) rate at 4 months (7%)	LA1: increase rate of EBF at 4 months to rate at 6 weeks (24%)	LA2: increase rate of EBF at 4 months to rate at 1 week (45%)	LA3: increase rate of EBF at 4 months to rate at birth (65%)
LB0: Exclusive breastfeeding (EBF) rate at 6 months (0.5%)	LB1: increase rate of EBF at 6 month to rate at 4-months (7%)		
LC0: 'any breastfeeding' rate at 6-months (25%)	LC1: increase rate of 'any breastfeeding' at 6-months to rate at 6-weeks (33%)		

Table 16.3: Estimation of potential savings per year for Lancashire in treating gastroenteritis in infants less than one year old, due to increase in variously defined breastfeeding rates (refers to 13,785 infants' first year of life)

Policy scenario	Base case estimates of:					
	Hospitalisation costs		Primary care costs		Total costs	
	Potential cost-savings per year	Potential cost-savings per infant per year	Potential cost-savings per year	Potential cost-savings per infant per year	Potential cost-savings per year	Potential cost-savings per infant per year
Policy A1	£28,715	£2.08	£4,327	£0.31	£33,042	£2.40
Policy A2	£77,941	£5.65	£11,746	£0.85	£89,687	£6.51
Policy A3	£118,963	£8.63	£17,928	£1.30	£136,891	£9.93
Policy B1	£13,332	£0.97	£2,009	£0.15	£15,341	£1.11
Policy C1	£40,382	£2.93	£7,144	£0.52	£47,526	£3.45

Lower respiratory tract infections (LRTI): The same economic model for LRTI developed in Section 4.3 of the main report was re-run to reflect Lancashire-specific input parameters, where available (Table 16.4).

Table 16.4: Lancashire-specific input parameters used in LRTI Economic Model*

Parameter	Value	Description	Source
Reference population	13,785 infants <1 year	Lancashire live birth totals after adjusting with Lancashire neonatal-mortality rate	ONS (2010)
Breastfeeding rates	EBF at 6-week: 24% Any breastfeeding at 6 week: 33%	Average across 5 PCTs, where data was available.	ChiMat Data Atlas
Rate of LRTI-related hospitalisations in <1 year	77.5 per 1000 infants <1 year	Hospitalisation rates due to LRTI and Bronchitis. Rate for the "North West" region	Infant Feeding Profile (2011)
Rate of LRTI-related GP consultations in <1 year	19,082 per 100,000 infants <1 year	GP consultations rate for clinical diagnosis of LRTI in children <1 year. Rate for the "North" region	RCGP (2010)

*All other input parameters unchanged.

Table 16.5: Lancashire-specific policy scenarios modelled

Definition of breastfeeding and rate used in base case:	Alternative policy scenarios modelled:		
LA0: Exclusive breastfeeding (EBF) rate at 4 months (7%)	LA1: increase rate of EBF at 4 months to rate at 6 weeks (24%)	LA2: increase rate of EBF at 4 months to rate at 1 week (45%)	LA3: increase rate of EBF at 4 months to rate at birth (65%)
LB0: Exclusive breastfeeding (EBF) rate at 6 months (0.5%)	LB1: increase rate of EBF at 6 month to rate at 4-months (7%)		
LC0: 'any breastfeeding' rate at 6-months (25%)	LC1: increase rate of 'any breastfeeding' at 6-months to rate at 6-weeks (33%)		

The expected difference in costs of caring for infants below the age of one year for LRTI following increases in breast feeding are presented as potential cost-savings.

Table 16.6: Estimation of potential savings per year <u>for Lancashire</u> in treating LRTI in infants less than one year old, due to increase in variously defined breastfeeding rates (refers to 13,785 infants' first year of life)

Policy scenario	Base case estimates of:					
	Hospitalisation costs		Primary care costs		Total costs	
	Potential cost-savings per year	Potential cost-savings per infant per year	Potential cost-savings per year	Potential cost-savings per infant per year	Potential cost-savings per year	Potential cost-savings per infant per year
Policy A1	£49,426	£3.59	£4,201	£0.30	£53,627	£3.89
Policy A2	£134,156	£9.73	£11,402	£0.83	£145,558	£10.56
Policy A3	£204,764	£14.85	£17,404	£1.26	£222,168	£16.12
Policy B1	£22,948	£1.66	£1,950	£0.14	£24,898	£1.81
Policy C1	£95,306	£6.91	£8,354	£0.61	£103,660	£7.52

Acute Otitis Media (AOM): The same economic model for AOM developed in Section 4.3 of the main report was re-run to reflect Lancashire-specific input parameters, where available (Table 16.7).

Table 16.7: Lancashire-specific input parameters used in AOM Economic Model*

Parameter	Value	Description	Source
Reference population	13,785 infants <1 year	Lancashire live birth totals after adjusting with Lancashire neonatal-mortality rate	ONS (2010)
Breastfeeding rates	EBF at 6-week: 24% Any breastfeeding at 6 week: 33%	Average across 5 PCTs, where data was available.	ChiMat Data Atlas
Rate of LRTI-related GP consultations in <1 year	13,740 per 100,000 infants <1 year	GP consultations rate for clinical diagnosis of LRTI in children <1 year. Rate for the "North" region	RCGP (2010)

*All other input parameters unchanged.

Table 16.8: Lancashire-specific policy scenarios modelled

Definition of breastfeeding and rate used in base case:	Alternative policy scenarios modelled:		
LA0: Exclusive breastfeeding (EBF) rate at 4 months (7%)	LA1: increase rate of EBF at 4 months to rate at 6 weeks (24%)	LA2: increase rate of EBF at 4 months to rate at 1 week (45%)	LA3: increase rate of EBF at 4 months to rate at birth (65%)
LB0: Exclusive breastfeeding (EBF) rate at 6 months (0.5%)	LB1: increase rate of EBF at 6 month to rate at 4-months (7%)		
LC0: 'any breastfeeding' rate at 6-months (25%)	LC1: increase rate of 'any breastfeeding' at 6-months to rate at 6-weeks (33%)		

The expected difference in costs of caring for infants below the age of one year for AOM following increases in breast feeding are presented as potential cost-savings.

Table 16.9: Estimation of potential savings per year for Lancashire in treating AOM in infants less than one year old, due to increase in variously defined breastfeeding rates (refers to 13,785 infants' first year of life)

Policy scenario	Base case estimates of **Primary care costs**	
	Potential cost-savings per year	**Potential cost-savings per infant per year**
Policy A1	£4,946	£0.36
Policy A2	£13,425	£0.97
Policy A3	£20,491	£1.49
Policy B1	£2,296	£0.17
Policy C1	£11,070	£0.80

Necrotising Enterocolitis (NEC): The same economic model for NEC developed in Section 4.3 of the main report was re-run to reflect Lancashire-specific input parameters, where available (16. 10).

Table 16.10: Lancashire-specific input parameters used in NEC Economic Model*

Parameter	**Value**	**Description**	**Source**
Reference population	13,829 live births	Lancashire live births	ONS (2010)

*All other input parameters unchanged.

Table 16.11: Lancashire-specific policy scenarios modelled

Definition of breastmilk feeding and rate used (2006) in base case:	**Alternative policy scenarios modelled:**		
Policy D0: Any breastmilk feeding rate at discharge in **neonatal units (35%)**	**Policy D1:** increase rate of any breastmilk feeding at discharge in neonatal units to 50%	**Policy D2:** increase rate of any breastmilk feeding at discharge in neonatal units to 75%	**Policy D3:** increase rate of any breastmilk feeding at discharge in neonatal units to 100%

The expected difference in costs of caring for infants below the age of one year for NEC following increases in breast feeding are presented as potential cost-savings.

Table 16.12: Estimated potential annual savings in NEC treatment costs due to increase in current breastfeeding rates <u>for Lancashire</u> (refers to 13,829 live births and 1,383 neonatal admissions)

	Total treatment costs per annum	Annual cost-savings per neonatal admission per year
Policy D1	£40,132	£29.02
Policy D2	£107,018	£77.39
Policy D3	£173,904	£125.75

Maternal breast cancer: The same economic model for maternal breast cancer developed in Section 4.3 of the main report was re-run to reflect Lancashire-specific input parameters, where available (Table 16.13).

Table 16.13: Lancashire-specific input parameters used in breast cancer Economic Model*

Parameter	Value	Description	Source
Reference population	5,504 primiparous women	Estimated first mothers in 2009 in Lancashire	ONS (2009) and Euro Peristat Project (2008)
Incidence of breast cancer	12500/100,000 population	Lifetime risk of breast cancer across Blackburn, Blackpool, Central, East and North Lancashire	National Cancer Intelligence Network (2012)

*All other input parameters unchanged.

Table 16.14: Lancashire-specific policy scenarios modelled

Definition of 'lifetime' breastfeeding and rate used (1996-2001) in base case:	Alternative policy scenarios modelled:		
Policy E0:	**Policy E1:**	**Policy E2:**	**Policy E3:**
32% primiparous women never breastfeeding; 36% breastfeeding for ≤6 months; 16% breastfeeding for 7-18 months; 16% breastfeeding for 18+months	Increase rate of breastfeeding for ≤6 months to 52% 16% never; 52% ≤6 mo; 16% 7-18 mo; 16% 18+ mo	Increase rate of breastfeeding for ≤ 18 months to 32% 16% never; 36% ≤6 mo; 32% 7-18 mo; 16% 18+ mo	Increase rate of breastfeeding for 18+ months to 32% 16% never; 36% ≤6 mo; 16% 7-18 mo; 32% 18+ mo

The expected differences in costs of caring for primiparous women with breast cancer following increases in breast feeding are presented as potential cost-savings and incremental benefit.

Table 16.15: Estimated potential savings in maternal breast cancer treatment costs due to increase in current breastfeeding rates <u>for Lancashire</u> (refers to 100,000 women)

Scenario E: Increasing current breastfeeding, as defined by 'specific' lifetime duration of breastfeeding	**Expected number of cases of breast cancer (lifetime)/ 100,000 primiparous women**	**Cancer cases avoided per 100,000 primiparous women over lifetime (relative to Policy E0**	**Incremental QALYs gained /100,000 primiparous women**	**Treatment costs saved/100,000 primiparous women**	**Benefit* (lifetime)/100,000 primiparous women**	**Incremental Benefit* (lifetime)/100,000 primiparous women**
Policy E0: current rates (i.e. 32% never; 36% ≤6 mo; 16% 7-18 mo; 16% 18+ mo)	12500	-			£453,905,752	-
Policy E1: Have half of never BF women to BF for ≤ 6 mo (i.e. 16% never; 52% ≤6 mo; 16% 7-18 mo; 16% 18+ mo)	12300	200	118	£4,887,076	£446,652,758	£7,252,994
Policy E2: Have half of never BF women to BF for ≤ 18 mo (i.e. 16% never; 36% ≤6 mo; 32% 7-18 mo; 16% 18+ mo)	12224	276	163	£6,746,386	£443,893,324	£10,012,428
Policy E3: Have half of never BF women to BF for 18+ mo (i.e. 16% never; 36% ≤6 mo; 16% 7-18 mo; 32% 18+ mo)	12138	362	214	£8,858,745	£440,758,335	£13,147,417

Appendix 17
Costs of going Baby Friendly

	Typical cost for maternity (2012 prices)	Typical cost for community (2012 prices)	Typical cost for university (2012 prices)
Accreditation			
Implementation Visit	£950	£950	N/A
Stage 1	£810	£810	£810
Stage 2	£3,150	£3,150	£2,700 (full assessment)
Stage 3	£4,150	£4,150	N/A
Training			
Breastfeeding and relationship building (in-house for 20 staff)	£5,600	£5,600	N/A
Place on Train the Trainer course	£690	£690	£690
Place on Project Management course	£405	£405	N/A
Place on Audit Workshop	£260	£260	N/A
Item			
Audit Tool	£290	£290	N/A

NB – This reflects an average of the types of costs different types of facilities may incur whilst working towards Baby Friendly accreditation. The costs for individual facilities may vary.