STUDY PROTOCOL

Exclusive human milk diet for very preterm babies in England: protocol for a cost-effectiveness and budget impact analysis [version 1; peer review: awaiting peer review]

Chris Sampson[1], Kyann Zhang[1], David Parkin[1,2], Grace Hampson[1]

[1]Office of Health Economics, London, SW1E 6QT, UK
[2]City, University of London, London, UK

v1 **First published:** 13 Jan 2021, **10**:21
https://doi.org/10.12688/f1000research.22450.1
Latest published: 13 Jan 2021, **10**:21
https://doi.org/10.12688/f1000research.22450.1

Abstract

Introduction: Babies born before 30 weeks' gestation are at increased risk of major clinical complications and have greater nutritional requirements. Where nutritional requirements cannot be sufficiently provided for by the mother's own milk (MOM), routine care in England uses cow milk-derived fortifiers and formulas. However, the use of cow milk in the diets of preterm babies has been associated with adverse health outcomes. Clinical trials have shown that an exclusive human milk diet (EHMD) – where MOM is supplemented by donor human milk-derived formulas and fortifiers – has the potential to be clinically beneficial and reduce the risk of complications.

Objectives: This study has two key objectives: 1) estimate the cost-effectiveness of an EHMD for babies born before 30 weeks' gestation, relative to routine care; 2) estimate the budget impact of adopting EHMDs in practice in England.

Methods: The analysis will use a modelling approach based on the most relevant data available. The population will consist of babies born in England before 30 weeks' gestation. Babies in the intervention arm will be simulated to represent outcomes associated with babies fed an EHMD, and those in the comparator arm to receive routine care. Model parameters will be drawn from three sources: i) a recently completed randomised clinical trial, ii) the National Neonatal Research Database, and iii) published literature. The model will adopt a time horizon of two years following initial admission to a neonatal unit. The primary outcome for the cost-effectiveness analysis will be the incremental cost per life-year gained (if observed) associated with the intervention, relative to the comparator. We will also present disaggregated outcomes in a cost-consequence analysis. The primary outcome for the budget impact analysis will be the total cost associated with EHMD compared with current practice from the perspective of the English National Health Service (NHS).

Open Peer Review

Reviewer Status *AWAITING PEER REVIEW*

Any reports and responses or comments on the article can be found at the end of the article.

Keywords
human milk, diet, neonatal, nutrition, cost-effectiveness, budget impact, preterm infants

Corresponding author: Chris Sampson (csampson@ohe.org)

Author roles: Sampson C: Conceptualization, Funding Acquisition, Methodology, Project Administration, Writing – Original Draft Preparation, Writing – Review & Editing; **Zhang K**: Conceptualization, Methodology, Writing – Original Draft Preparation; **Parkin D**: Methodology, Writing – Review & Editing; **Hampson G**: Methodology, Writing – Review & Editing

Competing interests: The authors assert that they have no known competing interests. The authors acknowledge that the products to be evaluated in this study are manufactured by the funder of the study.

Grant information: This study was commissioned and funded by Prolacta Bioscience.

How to cite this article: Sampson C, Zhang K, Parkin D and Hampson G. **Exclusive human milk diet for very preterm babies in England: protocol for a cost-effectiveness and budget impact analysis [version 1; peer review: awaiting peer review]** F1000Research 2021, **10**:21 https://doi.org/10.12688/f1000research.22450.1

First published: 13 Jan 2021, **10**:21 https://doi.org/10.12688/f1000research.22450.1

Background

Babies born before 30 weeks' gestation are at increased risk of major clinical complications including necrotising enterocolitis (NEC), sepsis, and mortality[1]. The clinical management of preterm babies is complicated by their having greater nutritional requirements than full-term babies. In many cases, the mothers' own milk (MOM) is not sufficient – in volume or nutritional content – to meet preterm babies' needs. Consequently, both preterm formulas and milk fortifiers are used to feed reterm infants.

In England, routinely used fortifiers and formulas are derived from cow milk. The use of cow milk-derived fortifier (CMDF) in the diet of preterm infants has been shown to be associated with several adverse health outcomes[2]. Clinical trials have demonstrated that an exclusive human milk diet (EHMD), based on a MOM alongside fortifiers and formulas manufactured from donor human milk, may be clinically beneficial[3,4]. An EHMD has been associated with reduced risk of negative sequelae such as NEC, sepsis, neurodevelopmental problems, and lung disease[5,6].

A randomised controlled trial was recently completed in England, sponsored by Newcastle Hospitals NHS Foundation Trust. The *Interactions between the diet and gut microbes and metabolism in preterm infants* (INDIGO) study sought to evaluate EHMDs in the English setting in terms of its impact on gut bacteria and body composition[7]. The INDIGO trial also recorded data relating to health care resource use and clinical endpoints.

An EHMD, where human milk-derived fortifier (HMDF) and formula are provided (where MOM is insufficient for the preterm infant's nutritional needs), is likely to be associated with higher upfront costs for the provision of nutrition. However, the major cost of neonatal care in England is attributable to time spent in a neonatal unit (NNU). If an EHMD reduced the time spent in the NNU, it could reduce costs overall.

Previous studies have evaluated the cost-effectiveness of an EHMD for low birth weight babies in the United States and found that it is likely to reduce mortality and reduce costs by reducing adverse clinical events[8–10]. However, there are important differences between the United States and the National Health Service (NHS) context in England, which mean that the findings may not be applicable. No previous studies have estimated the cost-effectiveness of an EHMD for low birth weight babies in England.

Methods

The aim of this analysis is to estimate the expected cost-effectiveness of an EHMD for preterm babies in England, and the budget impact of adopting its use in practice. The analysis will use a modelling approach based on the most relevant data available.

Population, interventions, and outcomes

The population will be babies born in England before 30 weeks' gestation, which aligns with the inclusion criteria used in the INDIGO trial. The population will represent a complete cohort of babies admitted to NNUs in England within one year.

Babies in the intervention arm are fed with MOM, supplemented with HMDFs (Humavant®+6 human milk fortifier [human, pasteurized], Prolacta Bioscience) with or without human milk-derived ready-to-feed preterm formula (Humavant® RTF 26 human milk-based premature infant formula, Prolacta Bioscience). The intervention arm is henceforth referred to as EHMD.

Babies in the comparator arm are fed with MOM, supplemented with CMDFs with or without cow milk-derived ready-to-feed formula. This comparator is intended to represent usual care in England, though usual care can vary between hospitals.

The cost-effectiveness analysis will estimate the cost per life-year associated with the intervention and comparator, using the best available evidence. If an EHMD is associated with improved outcomes and greater costs, its cost-effectiveness will be estimated as the cost per life year gained. This analysis will be conducted from the perspective of the NHS in England.

A secondary analysis will consider disaggregated outcomes in the form of a cost-consequence analysis. These outcomes will include counts of key events including death and several diagnostic indicators as described below.

As with the cost-effectiveness analysis, the budget impact of an EHMD will be estimated from the perspective of the NHS in England. This will be summarised as the total incremental cost based on health care costs associated with nutritional provision, and complications that incur service use. Costs will also be presented in a disaggregated form to guide decision-making at different levels (e.g. national and local).

The time horizon for the analysis will be two years from baseline, where baseline is initial admission to an NNU. Costs will be discounted at an annual rate of 3.5% for the cost-effectiveness analysis in accordance with methodological guidance published by the National Institute for Health and Care Excellence (NICE). Discounting will not be applied for the budget impact analysis.

Data and analysis

The overall approach for the analysis will be a model-based cost-effectiveness analysis. We will construct an individual sampling model to simulate clinical pathways and disease events for individual babies. The study is informed by published methods and reporting guidance, as set out in principles of good practice in state-transition modelling, budget impact analysis, and reporting for economic evaluations of health interventions[11–14]. The model will be developed using Microsoft Excel (Microsoft 365 version).

Model structure

We will develop a probabilistic discrete-time state-transition microsimulation. The cycle length for the model will be one day. We will conduct 10,000 Monte Carlo simulations for the

purpose of probabilistic sensitivity analysis. Each simulation will count the occurrence of events and sum costs over the time horizon.

The state-based transition model will have seven states, made up of four levels of neonatal care – intensive, high dependency, special, and transitional – inpatient hospital care, home, and death, as shown in Figure 1. Each state will be associated with a per-cycle cost. Each day in a neonatal care state will also be associated with a cost of nutrition.

Informed by the modelling exercise reported by Seaton *et al.*[15], we will assume that infants born before 30 weeks' gestation are transferred to one of three levels of neonatal care: intensive care, high dependency care, or special care, and that subsequent transitions are to lower levels of dependency. While this may not always be the case in practice, the key driver of health care costs is likely to be length of stay, rather than the specific pathway, and so we do not anticipate that this simplifying assumption will introduce substantial bias to our cost estimates.

Transitions are modelled from any neonatal care state to any post-discharge state. An unpopulated transition matrix is shown in Table 1.

A set of events can occur before a baby is discharged from neonatal care. Our model will include the following events:

- Surgical treatment for NEC
- Diagnosis of late-onset sepsis
- Diagnosis of short bowel syndrome
- Diagnosis of bronchopulmonary dysplasia (BPD)
- Diagnosis of retinopathy of prematurity (ROP)
- Diagnosis of neurosensory impairment

The probability of these events occurring will be assumed to be fixed across the different levels of care but to be potentially co-dependent on other events. For instance, the probability of short bowel syndrome and BPD will be associated with the occurrence and treatment of NEC. Stochastic occurrence of all

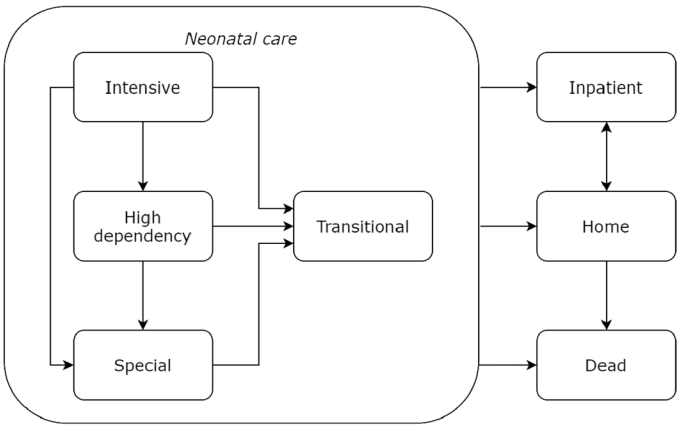

Figure 1. Model structure.

Table 1. Transition matrix. Black cells represent transitions with zero probability. White cells represent transitions with positive probability. Grey cells represent the probability of no transition.

To: / From:	Intensive care	High dependency care	Special care	Transitional care	Inpatient care	Home	Dead
Intensive care							
High dependency care							
Special care							
Transitional care							
Inpatient care							
Home							
Dead							

possible events will be recorded within each cycle of each simulation. Each event will be associated with a cost, if relevant.

Parameters

Table 2 shows the list of parameters that will be required by the model and their candidate sources. Transition probabilities, event probabilities, and diet-specific costs will depend on treatment allocation.

As part of the INDIGO trial, data were collected for participants, both directly and through the National Neonatal Research Database (NNRD). The variables available from the INDIGO trial are shown in Table 3.

Collection and analysis of variables as part of the INDIGO study was approved by the North East –Tyne & Wear South Research Ethics Committee (REC reference 17/NE/0169).

The key driver of total costs is likely to be the length of stay in the NNU. The INDIGO data will be used to estimate daily transition probabilities between different levels of care, assuming that babies are admitted to the highest level of care observed

Table 2. Model parameters.

Parameter	Anticipated source(s)
Baseline characteristics	
Population size	NNRD
Birth weight	NNRD
Gestation length (in weeks)	NNRD
Initial state	NNRD
Transition probabilities (dependent on allocation	
From intensive care	
To high dependency care	INDIGO
To special care	INDIGO
To transitional care	INDIGO
To inpatient care	INDIGO
To home	INDIGO
To dead	INDIGO, NNRD, literature[15]
From high dependency care	
To special care	INDIGO
To transitional care	INDIGO
To inpatient care	INDIGO
To home	INDIGO
To dead	INDIGO, NNRD, literature[15]
From special care	
To transitional care	INDIGO
To inpatient care	INDIGO
To home	INDIGO
To dead	INDIGO, NNRD, literature[15]

Parameter	Anticipated source(s)
From transitional care	
To inpatient care	INDIGO
To home	INDIGO
To dead	INDIGO, NNRD, literature
From inpatient care	
To home	INDIGO, NNRD, literature
To dead	INDIGO, NNRD, literature
From home	
To inpatient care	Literature
To dead	Literature
Event probabilities during NNU (dependent on allocation)	
Surgical treatment of NEC	Literature[2,16]
Diagnosis of late onset sepsis	Literature[2,6]
Diagnosis of short bowel syndrome (following NEC)	Literature[17]
Diagnosis of BPD	Literature[2,18]
Diagnosis of ROP	Literature[19,20]
Diagnosis of neurosensory impairment	Literature[21]
Resource use (dependent on allocation)	
Humavant+6 quantity per day	INDIGO
Humavant RTF 26 quantity per day	INDIGO
Formula quantity per day	INDIGO, literature[2]
Parenteral nutrition	INDIGO, literature
Humavant+6 price	Provided by Prolacta Bioscience
Humavant RTF 26 price	Provided by Prolacta Bioscience
Intensive care day	INDIGO, NHS Reference Costs
High dependency care day	INDIGO, NHS Reference Costs
Special care day	INDIGO, NHS Reference Costs
Transitional care day	INDIGO, NHS Reference Costs
Inpatient care day	INDIGO, NHS Reference Costs
Surgical interventions	INDIGO, NHS Reference Costs

Abbreviations: NNRD – National Neonatal Research Database; INDIGO – Interactions between the diet and gut microbes and metabolism in preterm infants (study); NNU – neonatal unit; NHS – National Health Service; NEC – necrotising enterocolitis; BPD – bronchopulmonary dysplasia; ROP – retinopathy of prematurity; RTF – ready-to-feed

Table 3. Interactions between the diet and gut microbes and metabolism in preterm infants (INDIGO) data items.

Data item	Description
Humavant+6 quantity	mL per day
Humavant RTF 26 quantity	mL per day
Formula quantity	mL per day
Parenteral nutrition	Number of days
Length of stay: intensive care	Number of days
Length of stay: high dependency care	Number of days
Length of stay: transitional care	Number of days
Surgical treatment of NEC	Yes/no
NEC diagnosis	Yes/no
Late onset sepsis diagnosis	Yes/no
Short bowel syndrome diagnosis	Yes/no
BPD diagnosis	Yes/no
ROP diagnosis	Yes/no
Mortality	Age at death

Abbreviations: RTF – ready-to-feed; NEC – necrotising enterocolitis; BPD – bronchopulmonary dysplasia; ROP – retinopathy of prematurity.

and are discharged from the lowest level of care observed, where intensive care > high dependency care > special care > transitional care. As described above, we do not anticipate that this assumption will introduce substantial bias to our cost estimates. Each transition probability will be derived from the rate at which babies leave each state.

The INDIGO data will also be used to estimate the cost of nutrition associated with each comparator, based on the quantity of Humavant+6 fortifier, Humavant RTF 26 premature infant formula, and other formula provided.

Key clinical inputs for this project will be sought through collaboration with clinical experts and from existing publications of previous research. Published sources used will include studies focusing on the prevalence and prognosis of complications associated with very premature babies (for example, (e.g. 21), as well as the outcomes of procedures (e.g. surgery) used to address these complications (e.g. 16). We will source papers that report estimates that most closely correspond to parameters required by our model, will use evidence from England wherever available, and will also prioritise more recent data over older data.

We will use NNRD data to define the population and to support external validation of our model. The extracted data items will be at the individual level, as described in Table 4.

The size of the population will be determined by the NNRD population, which we will assume to be equal to the number of eligible babies born in England for the one-year period from 1 January 2019 to 31 December 2019. Each baby simulated by the model will be attributed a birth weight and gestation length at birth, which will be used to determine the amount of feed required. The comparator group will be simulated to be of the same size and birth characteristics. The NNRD data will also define the proportion of babies allocated to intensive, high dependency, or special care at initial admission to the NNU.

We will compare our estimates with nationally representative data from NNRD to externally validate the estimates of our model with respect to clinical outcomes and resource use.

An application has been submitted to a national Research Ethics Committee for the use of NNRD data for the budget impact analysis. This study will involve analysis of data already collected by the NNRD, with no novel data collection or identifiable information used.

Cost-effectiveness

The time horizon for both the cost-effectiveness analysis and the budget impact analysis will be two years following admission to the NNU. Costs will be calculated from the perspective of the NHS using a combination of data from the INDIGO clinical trial and NHS Reference Costs.

The key outcome of the cost-effectiveness model will be the incremental cost per life-year gained for preterm babies fed with an EHMD, relative to those receiving standard care. Costs considered will include upfront costs associated with providing an EHMD, as well as costs of health care resource use associated with common clinical complications in preterm babies, including BPD and ROP. Only directly incurred costs associated with these clinical events will be included.

Budget impact

The budget impact will be calculated as the difference in total cost between a scenario where babies are fed an EHMD, and one in which CMDFs (with or without cow milk-derived read-to-feed formula) are used. Cost items included will be the same as those for the cost-effectiveness model.

The budget impact analysis will adopt a payer (NHS) perspective. The time horizon will be two years post-admission. The model will evaluate additional costs arising from the switch to a more expensive feeding regime against potential reductions in costs associated with lower health care resource use as a result of improved health outcomes and lower rates of complications (if observed).

The increase in costs associated with an EHMD consist of the additional (total) cost of human milk supplementation, which in turn will depend on the additional cost per day of human milk supplementation, the length of time supplementation is required, and the size of the target population. Cost reductions may arise from improved health outcomes for very preterm babies, with reductions in morbidity, surgical procedures (and associated complications), along with reduced length of stay in enhanced care facilities.

Table 4. National Neonatal Research Database (NNRD) data items.

Baby demographics (Standard)
Birth weight
Gestation length (at delivery)
Admission details
Primary category of care required on admission to neonatal critical care
Discharge details
Destination on discharge from neonatal critical care (level of care)
Transferred for further care type (level of care)
Receiving oxygen therapy on discharge indicator (Y/N)
Procedures recorded at discharge
Procedure (OPCS recorded on discharge from neonatal critical care)
Screening
Laparotomy for necrotising enterocolitis indication code (from abdominal x-rays)
Retinopathy of prematurity screening outcome status code
Daily care
Procedure (OPCS on neonatal critical care daily care date)
Parenteral nutrition received indicator
Enteral feed type given
Formula milk or milk fortifier type
Total volume of milk received
Sepsis suspected indicator
Patient level derived data items
Critical care length of stay
Diagnosis of BPD (NNAP definition)
Diagnosis of NEC (NNAP definition)
Diagnosis of neurodevelopmental impairments (NNAP definition)
Age at death

Abbreviations: NNAP – National Neonatal Audit Programme; NEC – necrotising enterocolitis; BPD – bronchopulmonary dysplasia

The overall budget impact will be presented as a net cost (or saving) to NHS England.

Sensitivity analyses

As a sensitivity analysis, we will conduct a within-trial analysis using only INDIGO trial data in combination with unit cost estimates.

Validation

Estimates generated by our model will be compared to estimates from NNRD as a means of externally validating our model. We will compare the following between NNRD and our model's estimates for the usual care arm:

- Mean length of stay in NNU
- Number of surgical NEC cases
- Number of diagnoses of ROP
- Number of sepsis diagnoses

Disseminations of information

Findings of this study will be published in a peer-reviewed journal or other publishing platform.

Study status. The study is in the initial planning stages, with early development of the model. The researchers have not yet accessed any data to be analysed as part of the study. Funding for the study is secured and the study has provisional approval from the Neonatal Data Analysis Unit (subject to ethical approval) to access NNRD data.

Discussion

This study is the first economic evaluation of EHMD use for very preterm babies in England. Given the potential for EHMD to reduce the incidence of health complications associated with significant costs to the health system – as shown in a previous evaluation for the United States – it may represent significantly reduced costs for the NHS and alleviate pressure on neonatal care resources. Beyond cost considerations, this intervention has the potential to bring about significant improvements in quality of life for preterm babies and, by association, their carers.

By using the results of a recent clinical trial for an EHMD in England, as well as costs specific to the English setting, the findings here will be highly relevant to decision-making about whether to use EHMD in the NHS. The inclusion of both a cost-consequence and budget impact analysis will allow us to illustrate a more comprehensive picture of the overall impact of an EHMD on the NHS.

Data availability

Underlying data

No data are associated with article.

Acknowledgments

We are grateful to Prof Nicholas Embleton for the expert opinion provided during the development of our study. Any errors or omissions are our own.

References

1. Patel RM, Kandefer S, Walsh MC, *et al.*: **Causes and Timing of Death in Extremely Premature Infants from 2000 through 2011.** *N Engl J Med.* 2015; **372**(4): 331–40.
PubMed Abstract | Publisher Full Text | Free Full Text

2. Abrams SA, Schanler RJ, Lee ML, *et al.*: **Greater Mortality and Morbidity in Extremely Preterm Infants Fed a Diet Containing Cow Milk Protein Products.** *Breastfeed Med.* 2014; **9**(6): 281–5.
PubMed Abstract | Publisher Full Text | Free Full Text

3. Sullivan S, Schanler RJ, Kim JH, *et al.*: **An Exclusively Human Milk-Based Diet Is Associated with a Lower Rate of Necrotizing Enterocolitis than a Diet of Human Milk and Bovine Milk-Based Products.** *J Pediatr.* 2010; **156**(4): 562-567.e1.
PubMed Abstract | Publisher Full Text

4. Cristofalo EA, Schanler RJ, Blanco CL, *et al.*: **Randomized Trial of Exclusive Human Milk versus Preterm Formula Diets in Extremely Premature Infants.** *J Pediatr.* 2013; **163**(6): 1592-1595.e1.
PubMed Abstract | Publisher Full Text

5. Buckle A, Taylor C: **Cost and Cost-Effectiveness of Donor Human Milk to Prevent Necrotizing Enterocolitis: Systematic Review.** *Breastfeed Med.* 2017; **12**(9): 528–36.
PubMed Abstract | Publisher Full Text

6. Hair AB, Peluso AM, Hawthorne KM, *et al.*: **Beyond Necrotizing Enterocolitis Prevention: Improving Outcomes with an Exclusive Human Milk-Based Diet.** *Breastfeed Med.* 2016; **11**(2): 70–4.
PubMed Abstract | Publisher Full Text | Free Full Text

7. Embleton N: **Interactions between diet and gut microbes in preterm infants**. ISRCTN; 2017 [cited 2020 Apr 16].
Publisher Full Text

8. Hampson G, Roberts SLE, Lucas A, *et al.*: **An economic analysis of human milk supplementation for very low birth weight babies in the USA.** *BMC Pediatr.* 2019; **19**(1): 337.
PubMed Abstract | Publisher Full Text | Free Full Text

9. Ganapathy V, Hay JW, Kim JH: **Costs of Necrotizing Enterocolitis and Cost-Effectiveness of Exclusively Human Milk-Based Products in Feeding Extremely Premature Infants.** *Breastfeed Med.* 2012; **7**(1): 29–37.
PubMed Abstract | Publisher Full Text

10. Johnson TJ, Patel AL, Bigger HR, *et al.*: **Economic Benefits and Costs of Human Milk Feedings: A Strategy to Reduce the Risk of Prematurity-Related Morbidities in Very-Low-Birth-Weight Infants.** *Adv Nutr.* 2014; **5**(2): 207–12.
PubMed Abstract | Publisher Full Text | Free Full Text

11. Sullivan SD, Mauskopf JA, Augustovski F, *et al.*: **Budget Impact Analysis-Principles of Good Practice: Report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force.** *Value Health.* 2014; **17**(1): 5–14.
PubMed Abstract | Publisher Full Text

12. Caro JJ, Briggs AH, Siebert U, *et al.*: **Modeling Good Research Practices--Overview: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-1.** *Value Health.* 2012; **15**(6): 796–803.
PubMed Abstract | Publisher Full Text

13. Husereau D, Drummond M, Petrou S, *et al.*: **Consolidated Health Economic Evaluation Reporting Standards (CHEERS)--Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force.** *Value Health.* 2013; **16**(2): 231–50.
PubMed Abstract | Publisher Full Text

14. Siebert U, Alagoz O, Bayoumi AM, *et al.*: **State-Transition Modeling: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force--3.** *Value Health.* 2012; **15**(6): 812–20.
PubMed Abstract | Publisher Full Text

15. Seaton SE, Barker L, Draper ES, *et al.*: **Modelling Neonatal Care Pathways for Babies Born Preterm: An Application of Multistate Modelling.** *PLoS One.* 2016; **11**(10): e0165202.
PubMed Abstract | Publisher Full Text | Free Full Text

16. Rees CM, Pierro A, Eaton S: **Neurodevelopmental outcomes of neonates with medically and surgically treated necrotizing enterocolitis.** *Arch Dis Child Fetal Neonatal Ed.* 2007; **92**(3): F193-198.
PubMed Abstract | Publisher Full Text | Free Full Text

17. Cole CR, Hansen NI, Higgins RD, *et al.*: **Very low birth weight preterm infants with surgical short bowel syndrome: incidence, morbidity and mortality, and growth outcomes at 18 to 22 months.** *Pediatrics.* 2008; **122**(3): e573-e582.
PubMed Abstract | Publisher Full Text | Free Full Text

18. Panickar J, Scholefield H, Kumar Y, *et al.*: **Atypical chronic lung disease in preterm infants.** *J Perinat Med.* 2004; **32**(2): 162–7.
PubMed Abstract | Publisher Full Text

19. O'Connor DL, Kiss A, Tomlinson C, *et al.*: **Nutrient enrichment of human milk with human and bovine milk–based fortifiers for infants born weighing <1250 g: a randomized clinical trial.** *Am J Clin Nutr.* 2018; **108**(1): 108–16.
PubMed Abstract | Publisher Full Text

20. Adams GGW, Bunce C, Xing W, *et al.*: **Treatment trends for retinopathy of prematurity in the UK: active surveillance study of infants at risk.** *BMJ Open.* 2017; **7**(3): e013366.
PubMed Abstract | Publisher Full Text | Free Full Text

21. Lui K, Lee SK, Kusuda S, *et al.*: **Trends in Outcomes for Neonates Born Very Preterm and Very Low Birth Weight in 11 High-Income Countries.** *J Pediatr.* 2019; **215**: 32-40.e14.
PubMed Abstract | Publisher Full Text